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ON THE ETIOLOGY OF TROPICAL DYSENTERY.[1]

By Simon Flexner, M. D.,

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There are few subjects in medicine that have attracted more attention than dysentery. Its history dates from the earliest written records and its ravages, unlike those of many of the pestilential diseases, have continued practically unaltered to the present day. The most ancient writing upon medicine—the papyrus Ebers—contains allusions to dysentery; the oldest Indian medical writers refer to it under the name "Atisar," while Herodotus speaks of its prevalence in Thessaly. Hippocrates, however, was the first to regard dysentery as an independent disease. I should hesitate to bring before this audience a subject so time-worn were it not for the fact that the nature and more especially the etiology of dysentery are among the problems that still await a satisfactory solution. Although the destructive epidemics which characterized the appearance of the disease in ancient times, and which were not unknown even as late as the last century, are in our own day encountered only as accompaniments of war and famine; nevertheless, dysentery still occurs in epidemic form in many Eastern and Western countries, while in the tropics the disease—not unlike cholera, another infectious disorder, the characteristic lesions of which are situated in the intestines—would seem to have found an endemic home.

Our imperfect knowledge of the nature of dysentery should be ascribed neither to lack of opportunity for the study of the disease nor to lack of energy in its pursuit. The literature contains some of the most distinguished names among clinicians and investigators, thanks to whose efforts its clinical history, its epidemiology, and, to a less extent, its pathological anatomy have received partial elucidation. Nor has the disease, in the past quarter of a century, escaped the attention of the bacteriologists, although it must be confessed that the results of somewhat extensive studies along these lines have been far less conclusive than might have been expected. Given a disease that is never entirely absent from temperate and tropical regions, that appears with epidemic severity, that permits of easy access to the *materies morbi*, one would certainly have been tempted to predict that the success achieved in so many other and apparently no less difficult fields, would probably be repeated. That the attempt to establish a common etiological factor for all cases of dysentery has thus far failed, this audience need not be reminded. That this failure has tended to emphasize the existence of several pathological states, for which the term dysentery is employed merely as the collective designation, need not be maintained here. But that these conclusions regarding the disease may after all not be in keeping with the facts is at least open to suspicion. When we recall the protean nature of other infectious diseases,

[1] Middleton-Goldsmith Lecture. Delivered before the New York Pathological Society, April 12, 1900.

among the most common of which are tuberculosis and typhoid fever, there can be no *a priori* objection to the hypothesis that the causative agent of dysentery need not necessarily vary for each of the many types of the disease that have, from time to time, been distinguished.

For the purpose of my inquiry, I shall consider briefly the clinical and pathological types, after which I shall ask your attention to the evidence for belief in specific causes. In considering this topic I shall endeavor to bring out the bearing of such studies upon dysentery in general and upon particular types of the disease. Finally, I shall hope to emphasize certain considerations connected with the etiology and pathology of dysentery by reciting some observations made upon the dysenteries prevailing in the Philippine Islands.

Types of Dysentery.—That the lines of demarcation between the several clinical and pathological types should be inaccurate is not a matter of wonder. Both the beginning and end of any given instance may vary widely, and the symptoms and lesions of cases arising sporadically in temperate climates may agree with those of dysentery occurring endemically in the tropics or epidemically in both localities. The terms "catarrhal," "tropical," "epidemic," and "diphtheritic," are far from signifying sharply-defined entities. The clinical manifestations and pathological lesions of the catarrhal variety occur in all kinds of dysentery and in all places where the disease prevails. Ever since the time of John Hunter there have been those who, upon pathological-anatomical grounds, have separated the endemic from the epidemic disease, and the line has been even more sharply drawn during the past decade, since the discovery of the Ameba coli in its relations to tropical dysentery. But the distinction between tropical dysentery and the epidemic disease is far from being sharp and constant. Diphtheritis and ulceration are not safe criteria. For while the former is commonly present in the epidemic disease, it occurs also in the tropical malady, and may, according to Kartulis, be associated with the ulcerative amebic variety, in which the lesions begin with destruction of the submucous coat of the gut.

As must always occur when classification of a disease proceeds upon clinical and pathological rather than etiological lines, the literature of dysentery is burdened with an interminable mass of appellations indicating the nature of the disorder or the author's conception of its pathological anatomy. Dysenteries, however, are now divided by the chief writers into several groups, depending upon the clinical history or the mode of prevalence. Thus Osler writes of 4 varieties, the acute catarrhal, the tropical or amebic, the diphtheritic, and the chronic dysentery. Davidson considers the subject under 2 headings: (1) according to prevalence—epidemic, endemic, the dysentery of war and famine; (2) upon clinical grounds—acute fibrinous or pseudodiphtheritic, and chronic dysentery. Kartulis describes endemic, epidemic and sporadic varieties; Manson speaks of a catarrhal and ulcerating dysentery, while Delafield distinguishes in the environs of New York at least 5 distinct types of this disease, only one of which would appear to be due to a specific agent—the Ameba coli.

Evidences for Specific Causes. Bacteria.—The presence of bacteria in the stools and tissues in dysentery was demonstrated by Klebs, Prior and Ziegler, whose studies, carried out upon the epidemic disease, have now only a minor historical interest, although Ziegler still holds that the relations of certain bacilli to the lesions speak for their pathogenic action. The early studies of Hlava upon the epidemic disease yielded quite inconclusive results, since, although he was able to obtain as many as 19 different kinds of bacilli in cultures, inoculations into animals failed entirely to reproduce the morbid process. Chantemesse and Widal were somewhat more fortunate. From five cases of tropical dysentery they obtained a bacillus which, when injected into the stomach or rectum of guinea-pigs, gave rise to diphtheritis, an observation which Grigoriew, who believed that he had isolated the same microorganism from 10 cases of dysentery, failed to confirm.

Maggiori, who studied 11 cases of the epidemic disease, obtained B. coli communis regularly and in large numbers. Less frequently B. proteus vulgaris was isolated, while in some cases the pyogenic cocci and B. pyocyaneus were found. This investigator considered it highly probable that the disease was caused by a Bacillus coli of intensified virulence—a conception also shared by Laveran, Arnaud, Celli and Fiocca and Escherich, who isolated the same organisms from dysenteric cases. Arnaud's series was larger, embracing 53 acute cases occurring in Tunis, from all of which B. coli was isolated. The spleen of a fatal case also yielded him the organisms. The ingestion of cultures in the case of several kinds of animals gave no results; while rectal injections of bouillon cultures, previously raised to 60-80° C., produced in two dogs a fatal and characteristic dysentery—a result in striking opposition to those reported by other writers.

The studies upon this bacillus by Celli and Fiocca are the most important which we possess. Their cases numbered 62 and included examples of the sporadic, epidemic, and tropical disease occurring in Italy and Egypt. From the fact that especial attention was paid to the occurrence and action of the Ameba coli, the results of these authors are doubly useful. They exclude this organism as the cause of any form of the disease and consider that a variety of the colon-bacillus, of especial virulence, which they designate B. coli dysenteriæ, is responsible for the lesions. Along with this colon-bacillus they found typhoid-like bacilli and streptococci. Their experiments upon animals are also more conclusive than any others. With cultures they were able to produce dysentery in cats, and while they admit that other microorganisms were also capable of producing similar results, they found that the latter acted far less constantly than their dysenteric bacillus. A toxin separated from growths of the organism was found to give rise to similar conditions. Celli, in another publication, expresses the view that it is this toxin that first exerts an injurious effect upon the intestinal mucosa, after which the destructive lesion is produced by the pyogenic cocci. Results similar to those of Celli were obtained by Del Pino and Alessandri. The latter, working on a case of postoperative dysentery, secured cultures of B. coli that yielded a toxin

capable of setting up dysentery in young cats. In their most recent paper, Celli and Valenti describe the production in dogs of sera, which, when tested upon experimental animals, exert a protective and healing effect. Upon human beings its action was not equally positive.

The colon bacillus is also believed by Escherich to play an important part in the production of a contagious enteric disorder (colitis contagiosa) in children. In its morbid anatomy the disease agrees with catarrhal dysentery.

The bacilli thus far enumerated, except those of Chantemesse and Widal, so far as they could be studied in cultures, have shown no specific properties. They all represent a well-known bacterial species, constantly present normally in the situation from which the organisms were obtained in disease, and whose only unusual properties were increased virulence when tested upon animals, and a capacity to set up enteritis when injected into the intestines of dogs and cats.

The investigations of an epidemic of dysentery which prevailed in Japan yielded different and apparently more convincing results. Ogata isolated fine bacilli, which liquefy gelatin, stain by Gram's method, and set up, when introduced by the mouth or by the rectum into guinea-pigs and cats, intestinal ulcerations. The organism regarded by Ogata as the cause of epidemic dysentery was isolated from 23 cases of the disease occurring in Padua by Vivaldi. Since that time it appears not to have been found again.

This list does not entirely cover the bacillary species isolated from cases of dysentery. The recent publication of Shiga, who also studied the disease prevailing in Japan, is needed to complete the number. But as this investigator's studies have a very direct bearing upon my own, I shall defer speaking of them for the present.

On the other hand, a causative rôle in the production of dysentery has also been ascribed to the pyogenic cocci. Besides being found in association with bacilli, by several of the investigators already mentioned, they have been regarded as the chief pathogenic agents by Zancarol, whose studies were carried out in Alexandria, by Silvestri of Turin, by Bertrand and Baucher of France, and very recently by Ascher, who investigated cases arising in Eastern and Western Prussia. These cocci, especially the streptococci, were capable in certain instances (Silvestri, Ascher) of setting up, in cats, dysentery, and liver-abscess. The cocci isolated by Ascher were also said to have shown the agglutination reaction with the blood-serum of the patients from whom they were obtained. As a cause of a special variety of endemic dysentery —the endemic enterocolitis of Cochin China—Calmette obtained the Bacillus pyocyaneus. The same microorganism was isolated, from a small epidemic of the disease occurring in New York State, by Lartigau, in another epidemic in children, prevailing in Canada, by Adami, and in certain sporadic cases of gastric and enteric infection, by L. F. Barker in Baltimore.

Protozoa.—Because of the great diversity of the normal intestinal flora the varieties of bacteria which can be isolated from the dejections and intestinal contents are relatively numerous. The differences in the numbers and kinds of bacteria capable of flourishing there, rendered possible by the existence of pathological conditions, readily account for many of the results of the bacteriologic studies given. With animal microparasites the case is different. Protozoa do not exist in easily demonstrable forms or numbers in the dejecta in health, and the number of species occurring under all conditions is small. Of these the list is confined to a few kinds of flagellates—which even when present in considerable numbers do little harm—and the amebæ.

It is to the rôle of the amebæ—a particular variety of which has achieved the distinction of being connected in a causal relation with endemic dysentery—that I wish to direct your attention. Since the studies of Kartulis, Councilman and Lafleur, and Kruse and Pasquale, so firmly has the idea of this connection taken hold of the popular medical mind, that the designation "amebic" as synonymous with "endemic" or "tropical" dysentery has been widely adopted. And yet the evidence upon which this belief is based cannot be regarded as convincing. Until we shall have gained means of differentiating amebæ other than those we now possess, and, moreover, until we are able to control their development with at least as great perfection as in the case of bacteria, the question of the precise part played by them in dysentery cannot be satisfactorily determined.

Since the historical observation of Lambl upon the occurrence of amebæ in the dejections of human beings, and especially since the confirmatory observations of Cunningham, Lewis and R. Koch, our knowledge of the distribution of these organisms in human beings has constantly widened and deepened. It was, moreover, the study by Lösch of a case of dysentery in which an ameba, called by him Ameba coli, occurred that gave the impulse to the investigation of the pathological actions of such organisms.

The importance of amebæ was further enforced by the demonstration of the organisms in sections of dysenteric ulcers by R. Koch, first in Egypt and afterwards in India. Following these successes, and probably directly through the suggestion of Koch, Kartulis began his series of observations and publications, which more than any other similar writings have tended to isolate tropical dysentery and place it upon a probable etiological basis.

The work of Kartulis need not be reviewed in detail in this place. His conclusion that in every undoubted case of dysentery occurring in Egypt the amebæ are present, has not been entirely confirmed. That they are, moreover, never present in the intestines in other enteric diseases and in health has also not been the experience of all other investigators. But that amebæ are abundant in many cases of tropical dysentery and may also be demonstrated in the contents of the hepatic abscess in the disease, the studies of Kartulis and those of subsequent investigators have definitely shown.

To follow the list of discoveries in cases of dysentery which have accumulated in the last decade is unnecessary and would carry us too far afield. Reports confirmatory of the results of Koch and Kartulis have appeared from many European

countries, the Pacific Islands, and from both North and South America. Ten years have, however, seen a modification of the views regarding amebæ, as causes of pathological conditions in human beings. The demonstration of amebæ, indistinguishable from the Ameba coli, in various intestinal diseases and even in healthy persons, has necessitated a recasting of the exclusive belief in their pathogenicity and relation to dysentery.

That amebæ may exist in diseases other than dysentery was conclusively proven by the early observations (Cunningham, Lewis) upon choleraic discharges. More important results were obtained by Grassi, first in 1882 and later in 1888. He describes amebæ which may occur, in considerable numbers, in diseases as varied as typhoid fever, cholera, pellagra, and colitis secondary to tumors. He demonstrated their presence in diarrheas and dysenteries, but at times also found them in the dejecta of healthy individuals. That amebæ can exist in the intestines without any disturbance of the health of their host was, therefore, definitely established by Grassi's observations as well as by those of Calandrucci, Massiutin, Kruse and Pasquale, Gasser and Schuberg. The observations of the last-named investigator are especially valuable, in that he showed that to the reaction of the lower colon and the consistence of the feces was due the fact that amebæ could not be constantly found with comparative ease in the dejecta. If a laxative, as for example, Carlsbad salts, is administered and the contents of the upper colon are then collected and examined, amebæ are frequently demonstrable. Moreover, under these conditions flagellates—the trichomonas and cercomonas—appear in the stools. He looks upon these parasites as common commensals in man.

It can, therefore, no longer be held that amebæ are necessarily pathogenic when found sojourning in the intestine in man. Indeed, the necessity of recognizing distinct species of amebæ had already begun to force itself upon thoughtful students, who until lately believed in their constant pathogenic action. Quincke and Roos, who observed amebæ first in a healthy individual, and later in two widely dissimilar cases of enteritis, tested the different organisms concerned for pathogenesis upon cats. From their results they believed that according to certain structural differences, and the action of the parasites in engulfing red blood-corpuscles, two main varieties or species can be distinguished, the one phagocytic for red blood-corpuscles and pathogenic for man and cats—this species being identical with the Ameba coli of Lösch—the other, nonpathogenic and nonphagocytic for blood-corpuscles, which they designate A. coli mitis. According to this view A. coli, A. felis, and A. dysenteriæ of Councilman and Lafleur are all one species; A. coli mitisis a harmless saprophyte, or at least is one of relative pathogenic insignificance.

It requires no elaborate argument to bring out the fallacies of such a method of distinction. Results following the introduction of so complex a material as dejecta into an animal cannot be accepted as deciding the properties of any single constituent. What has already been said concerning the ability of pure bacterial cultures to produce enteric lesions affords a sufficient criticism of such a procedure.

That amebæ when combined with bacteria may cause intestinal lesions and even ulceration is now established. Furthermore, the experiments of Kartulis and Kruse and Pasquale with the contents of hepatic abscesses, supposed to be free from bacteria, are all but convincing, in so far as they may be supposed to prove the capacity of amebæ alone to set up such changes.

The attempt to cultivate the Ameba coli without admixture of bacteria has in all probability never yet been successfully carried out. The supposed positive experiment of Kartulis is now known to have been erroneous. Whether Celli and Fiocca have succeeded is still doubtful. In any case no satisfactory experimental production of amebic dysentery in cats or other animals has thus far been achieved with cultures of amebæ free or relatively free from bacteria.

The pathological findings in amebic dysentery have been adduced as proving its specific character by Councilman and Lafleur, Kruse and Pasquale and Kartulis. According to this view the intestinal ulcers in amebic dysentery begin as in infiltration of the submucous coat that leads to necrosis of the overlying membrane. The lesions, unless complicated by the presence of bacteria, are free from the products of purulent inflammation. The accompanying abscess of the liver exists independently of the presence of bacteria. Kruse and Pasquale, and Kartulis ascribe greater significance to bacterial association than do Councilman and Lafleur. Kartulis sees in the occasional diphtheritis evidence of their action, while Kruse and Pasquale have followed them in their penetration into the coats of the gut, where they lie side by side with the amebæ or even precede them in the invasion. Both bacilli and cocci occur; and wherever necrosis is found, bacilli are sure to occur in groups and masses. "The amebæ and bacilli together start the lesions in the intestine." (Kruse and Pasquale.)

The form of lesions here described does not entirely represent the disease as it appears in the tropics. Even Lafleur in a later communication says that the term "tropical" can be used only as a partial synonym for amebic dysentery, inasmuch as, on the other hand, the disease, though more frequent in the tropics, is by no means limited to those regions, while, on the other hand, there are undoubted cases of dysentery in the tropics which are not of the amebic form—a statement borne out by my own observations.

How far, then, have the foregoing results aided us in clearing up the hitherto obscure etiology of this protean malady? While epidemic, endemic, and sporadic dysentery have been subjected to bacteriological investigation, the chief work thus far done has been with the tropical variety. Although the actual number of cases of the epidemic disease which have been carefully studied is small, it is significant that, with two exceptions—the studies of Ogata and Calmette—the several different microorganisms isolated have all been bacteria which are normally present in the intestinal canal. The cultures have, it is true, undergone changes of virulence, but in other respects they have retained their ordinary biological and physiological properties unaltered. It would certainly seem *a priori* highly improbable that so severe and devastating a

disease as epidemic dysentery should be due to microorganisms which are constant inhabitants of the intestinal tract. Moreover, when it is recalled how easily and under what great variety of conditions such accessions of virulence may be achieved, it would be remarkable that epidemics of dysentery are, nevertheless, relatively rare phenomena.

Turning to the tropical disease, we also observe that several microorganisms have been assigned as the causative agent. Chantemesse and Widal have described a bacillus not obtained since from similar cases; Arnaud, Laveran, and Celli and Fiocca have seen in the colon-bacillus, modified in its pathogenicity, a sufficient cause. More weight, and with far greater justice, has been laid upon the Ameba coli. But this organism has been found more especially in chronic cases. Kartulis states that the catarrhal stage, which is common in the epidemic and sporadic disease, is uncommon in this form. If the Ameba coli is the organism most commonly present in the acute dysenteries of the tropics, the fact has not yet been conclusively established. However this may be, in Manila, where the organism is not infrequently present in the chronic disease, its absence in the very acute and often rapidly fatal cases of dysentery must be regarded as of significance.

From the preceding considerations the following conclusions seem warranted:

1. No bacterial species yet described as the cause of dysentery has an especial claim to be regarded as the chief microorganism concerned in the causation of the disease.

2. It is unlikely that any bacterial species that is constantly and normally present in the intestine or in the environs of man, except where the disease prevails in an endemic form, can be regarded as the probable cause of epidemic dysentery.

3. The relations of sporadic to epidemic dysentery are so remote that it is improbable that the two diseases are produced by the same organic cause.

4. The pathogenic action of the Ameba coli in many cases of tropical, and in certain examples of sporadic, dysentery, has not been disproved by the discovery of amebæ in the normal intestine and in diseases other than dysentery. While amebæ are commonly present and are concerned in the production of the lesions in subacute and chronic dysentery, they have not thus far been shown to be equally connected with the acute dysenteries even in the tropics. In the former varieties, bacterial association probably has much influence upon the pathogenic powers of the amebæ.

The Dysentery of Japan and the Philippine Islands.

Every year, especially in the summer and autumn, dysentery prevails in Japan. Ogata and Eldridge have given the statistics of incidence and mortality in the years from 1878 to 1899:

Year.	Cases.	Deaths.
1878	1,118	206
1879	8,322	1,487
1880	5,047	1,305
1881	7,001	1,837
1882	4,330	1,313
1883	21,172	5,066
1884	22,702	6,036
1885	47,377	10,690
1886	24,328	6,839
1887	16,125	4,244
1888	26,789	6,570
1889	22,893	5,970
1890	42,632	8,706
1891	46,358	11,208
1892	70,842	16,844
1893	167,305	41,282
1894	155,140	38,094
1895	52,711	12,959
1896	85,876	22,356
1897	91,077	23,189
1898	90,933	22,379
1899	125,989	26,709
	1,136,067	275,289

The epidemic studied bacteriologically by Ogata occurred in the province of Oita where in 1890, 801 cases occurred with 221 deaths, and in 1891, 8390 cases with 2163 deaths—an average mortality of from 26 to 27 per cent. This epidemic had been preceded by sporadic cases in the previous winter, and in its spread showed a striking contagious character. The lesions in the intestine are described in one case, death having taken place on the eleventh day of the disease. The lower segment of the small intestine was hyperemic. The large intestine was greatly swollen so that the lumen was almost obliterated. The mucous membrane was hyperemic and presented a deep bluish-red color. The contents were chocolate-colored. The mucosa of the transverse and descending colon, and especially of the sigmoid flexure, showed small ulcers, the size of peas, which were so numerous as to give to the membrane a sieve-like appearance. They were also found, though in smaller numbers, in the descending colon and rectum. No large ulcers were present. The peculiar bacilli—staining by Gram, liquefying gelatine, and causing in animals, whether injected beneath the skin or into the rectum, hyperemia and ulceration of the intestinal mucosa—have been already described. Ogata's decision was that the bacillus isolated was probably the cause of the epidemic of dysentery prevailing in Southern Japan.

I am not acquainted with a full description of the morbid anatomy of the dysentery prevailing in Japan. Schaube formerly of Tokio, in his "Die Krankheiten der warmen Länder," does not give a detailed account of the Japanese variety, but contents himself with the usual classification and description of the disease. The meager accounts may possibly be explained by the fact that necropsies are obtained in Japan only with great difficulty. Dr. Eldridge states that the lesions seen in "amebic dysentery" as described by Councilman and Lafleur are seldom met with. The common lesions are destructive, progressing from the surface downwards, associated with necrosis of the mucosa and croupous infiltration (diphtheritis). Perforation is unusual, the muscular coat offering a strong resistance to the pathological process.

The most recent bacteriological study of dysentery has been made by Shiga, to whose results I would ask especial attention. During 1897 the disease prevailed epidemically in Japan, 89,400 cases with 22,300 deaths (24 per cent) being recorded from June to December. Out of a considerable number of cases occurring in Tokyo, 36 were subjected to bacteriological examination by Shiga.

As was readily recognized by him, four points must be proved in the effort to show that an organism suspected of standing in etiological relation to any given disease is really the causative agent: (1) The organism must occur constantly; (2) it must be a species not present normally in the diseased part; (3) it must be pathogenic and produce in experimental animals lesions similar to those from which it was obtained; (4) it should in virtue of its pathogenic activity in man show the Widal agglutination reaction with the blood-sera of those who have suffered from the disease. From the series of cases examined there was obtained from the dejecta and intestinal contents and walls, and from the mesenteric glands, a bacillus which fulfilled all these requirements and which was regarded as the cause of Japanese dysentery, at least.

Before entering upon a description of this organism I should like to direct your attention to the dysentery prevailing in the Philippine Islands, especially in and around Manila. The report of the Surgeon-General of the Army for 1899 contains a tabulation of diseases, observed among the American troops, during the first four months of the American occupation of Manila. In it the dysenteries are included with the diarrheal diseases. The total number of cases reported is 445, the death-rate being 0.48 per cent. The comment made is that "the malarial diseases exceed their prevalence in the United States in the proportion of 370 to 96, and the diarrheal diseases in the proportion of 445 to 116, or about 4 to 1 in both instances."

This compilation fails to give an adequate idea of the extent, severity, and mortality of dysentery in Manila. Although, unfortunately, figures are not obtainable, I am convinced, after nearly three months' residence in Manila, that the enteric diseases, of which dysentery was the most frequent and important, were the chief causes of disability and mortality among the land forces of the American army.[1]

The disease appears in two main forms, acute and chronic dysentery. The stools and intestinal contents at autopsy were scrutinized for amebæ. So far as regards the acute cases these organisms were absent or very difficult to find in the fresh stools and in the intestinal contents immediately after death. In the chronic forms of the disease ulcers were present in the mucosa and submucosa; the lesions were confined to the large intestine, the coats of which were greatly thickened; at times large sloughs of the mucous membrane, partly detached, were encountered. Amebæ were commonly present, but were variable as to actual occurrence and numbers. Large hepatic abscesses, usually single, were encountered in a number of these cases. Amebæ were not always found in the contents of these abscesses; sometimes bacteria were present alone or associated with amebæ. Amebæ not distinguishable, except by the absence of specific inclusions, from those in the stools of human cases exist in the dejecta of monkeys liberated from captivity and now at large in Manila.

The morbid anatomy of the chronic disease agrees in part only with that of "amebic" dysentery. I shall draw attention later to another form of the chronic disease.

The pathological changes in the acute cases differ widely from those of the chronic affections. I shall now give in brief the condition of the intestines in several cases of acute dysentery. The patients were American soldiers.

Case 1.—Death on the sixth day of the disease. The entire large intestine from the cecum to the rectum is dilated and the walls of the gut are thickened. The mucous membrane is swollen, its consistence is much increased and the normal folds are thrown into elevated, coarse corrugations. The general color of the mucous membrane is deep red, but there are present many brighter spots evidently due to hemorrhage. No distinct false membrane is to be made out, but here and there are scattered white elevations, which, after the intestine has been washed, become more prominent and can be removed only with some difficulty, small defects in the membrane being left behind. In the fresh state ulceration was not made out, but after the washing referred to, there are found in the lower portions of the sigmoid flexure minute, sieve-like points, with perfectly sharp edges, representing defects which lead into the submucosa. The smallest of these openings are the size of pin-points, the largest about 2 mm. in diameter. The contents of the intestine showed no amebæ.

Case 2.—Death on the fifth day of illness. The small intestine, excepting the lower end of the ileum, which is deeply congested and swollen, shows no alteration. The serosa over the large intestine is injected, but is otherwise normal. The large intestine is much thickened and its consistence is increased. On opening the gut the contents are found to be dark or nearly black in color, an appearance probably due to the administration of bismuth. The mucous membrane extending from the rectum to the ileocecal valve, and beyond the valve in the ileum for a distance of 4 cm., is congested, swollen, and hemorrhagic. Scattered here and there on the surface are elevated, white, irregular points and small, flattened areas, which suggest a pseudo-membrane, but which cannot be absolutely identified as of such a nature. The normal velvety character of the mucous membrane is lost. No ulceration can be made out and the lesions seem to be chiefly in the mucosa and submucosa. Particularly conspicuous is the wide diffusion of the lesions, no part of the mucous surface within the limits defined having escaped. The mesenteric glands are congested and moderately swollen. Although amebæ had been found in the evacuations two days previous to death, they could not be demonstrated in the intestinal contents at autopsy.

Case 3.—Death after an illness of 6 days. The large intestine is markedly dilated and the serous coat is much injected. The contents of the large intestine are represented by a grumous, pink, pulpy material. The mucous membrane is swollen and hyperemic, and presents a striking granular appearance due to exudate upon the surface; many areas of hemorrhage are also observed. The entire mucosa of the large intes-

[1] The studies on dysentery here recorded were made by a commission consisting of Dr. L. F. Barker and myself, sent out by the Johns Hopkins University to study the diseases prevailing in the Philippine Islands. To this commission were attached Messrs. Joseph M. Flint and Frederick P. Gay, who were, at that time, members of the Johns Hopkins Medical School.

tine is implicated in this process. Ulceration is not present. The mesenteric glands are swollen, congested, and hemorrhagic. The spleen is moderately enlarged. Amebæ were not demonstrable in the intestinal contents.

The three cases which have been selected do not agree with amebic dysentery as hitherto described. In only one were amebæ found in the stools, and even then they could not be demonstrated in the intestinal contents, obtained immediately after death, which took place two days after the first examination. The stools consisted, as was the rule in the acute disease observed in Manila, of mucus and blood. The microscopical examination revealed epithelial cells, red blood-corpuscles, a moderate number of bacteria and many amebæ. On the same day injections of quinin were begun, ipecac being administered by the mouth. The note 24 hours later states that the stool contained mucus but less blood. Epithelial cells were still present and the bacteria appeared in greatly increased numbers. No amebæ could be discovered. Death took place on the day of this examination.

In their pathological histology also the acute dysenteries differ from the amebic form. The histological changes appear in the mucous membrane, submucosa and muscularis, being most marked in the former situations. Those of the mucous membrane consist of coagulative necrosis with exudation of fibrin and polymorphonuclear cells. The fibrinous and cellular exudate may entirely replace the glandular layer, or here and there a gland may be preserved. The pseudomembrane is a close-meshed network of fibrin enclosing multinuclear, often fragmented, cells. No blood-vessels are to be distinguished, but a variable number of red blood-corpuscles are mingled with the exudate and lie free upon the surface. The muscularis mucosa is not always distinguishable—indeed it is frequently lost in the exudate. The submucosa is always much altered. From the changes found in it, it is evident that to them is chiefly due the thickening of the gut. The part most affected is the layer next the muscularis mucosa. Here are found hemorrhages of variable size, while in the interstices of the tissues some fibrin appears. More marked, however, are cellular accumulations, which are present, not uniformly, but in irregular areas. The deeper layers of the submucosa show similar cellular infiltrations, although the amount is less striking. On the other hand, at these levels the quantity of fibrin is greatly increased and hemorrhages are numerous.

The character of the cellular exudate is quite uniform. Excluding the red blood-corpuscles, the new cells consist chiefly of plasma cells. These are collected into foci, often about blood-vessels, veins and arteries, but sometimes occur in small groups or singly. There can be no doubt that these are identical with Unna's plasma cells; they show the reticulated nucleus, often placed eccentrically, and the fine blue granulations of cell-protoplasm in eosin and methylene-blue staining. As the deeper levels of the submucosa are reached, hemorrhages and fibrin are abundant. The size of the foci of plasma cells gradually diminishes. At the muscular border they have about disappeared. Among the plasma cells a variable number of eosinophilic cells may be distinguished.

In the submucosa, infiltration, hemorrhage and fibrin-formation take place also beneath an intact or almost intact mucous membrane. The nature of the cellular infiltration may be identical with that already described, but in addition accumulations of lymphoid cells may frequently be seen. These exist in the layer of the submucosa immediately next the muscularis mucosæ; the deeper cells resemble plasma cells.

The blood-vessels of the submucosa may be patent and congested, the blood containing an excess of white elements; or they may show recent leucocytic and fibrinous thrombi. Hyaline degeneration of the vascular walls was not encountered. Large spaces in the submucosa may contain fibrinous clots; these are probably dilated and thrombosed lymphatic vessels.

The muscular coat shows only hemorrhages, which may be of large size, although they are usually smaller than in the submucosa. The peritoneal tunic is usually unaltered.

From this brief description it is evident that the main pathological changes take place in the mucous membrane and submucosa and it is also clear that the 2 tunics may be affected simultaneously or the submucosa may suffer pathological alterations without involvement of the mucosa. So far as could be ascertained from the material studied, in contradistinction to the condition observed in "amebic" dysentery, ulceration did not begin in the submucosa, but any defect which may have occurred resulted from exfoliation of the necrotic mucosa and the attached pseudomembrane.

It is interesting in this connection, to emphasize the fact that the polymorphonuclear leucocyte plays a very insignificant rôle in the process of infiltration in the submucosa, whereas in the affected mucous membrane it is much in evidence. On the other hand, the blood-vessels of the submucosa contain those cells in increased numbers and the cellular and fibrinous thrombi are rich in them. It would appear, therefore, that these cells do not leave the vessels in the submucosa as readily as those of the mucous membrane. That the blood-vessels of the submucosa suffer great injury from the pathogenic agent is shown by the free hemorrhages and the fibrinous exudation.

Bacteria are abundant in the fibrinous exudation in the mucous membrane. The chief varieties distinguishable are cocci and bacilli. In specimens stained by Gram's or Weigert's methods, large numbers of cocci, in short chains and groups, can be made out. In other specimens, stained in Unna's alkaline methylene-blue, besides the cocci many bacilli may be seen. These are quite uniform in size; they present the morphological characters of the colon-typhoid group, from which they could not be distinguished in sections of tissue. While the bacteria are so abundant in the necrotic mucous membrane, diligent search failed to exhibit either bacilli or cocci in the infiltrated areas of the affected submucosa. The conviction is therefore forced upon one that the lesions in the submucosa are toxic in origin. Amebæ were not discovered in the sections.

The Bacteriology of Philippine Dysentery.

In the study of the bacterial flora of the disease acute and

chronic cases were utilized. The methods of procedure varied only slightly in different cases. The acutely ill being in bed, the evacuations were collected in bed-pans, which a short time before had been carefully scalded. The patients who were about the wards were taken to the laboratory, where cultures could be made immediately from the contents of the rectum. The fatal cases were subjected to autopsy immediately after death. The large gut at different levels was burned through with a hot knife, and cultures were made before disturbing any of the viscera. Plate cultures in agar-agar were employed. The average number of plates made from a single case was twelve. The material was mixed with bouillon, so as to afford the advantage of a relatively large amount for plating. It was frequently obtained from several different portions of the evacuation or from several levels of the intestine. Only such plates as contained well-separated colonies were utilized. Control microscopical examinations of the evacuations and intestinal contents were made. It may be mentioned that cercomonades and trichomonades were very common in the diarrheal stools. They did not appear to be of pathological significance.

From the separated colonies, agar-slant cultures were made. The growths of the pyogenic cocci as well as those of B. pyocyaneus were not pursued further. The former was never absent, the latter was rarely present. The bacillary colonies, which occurred with regularity in the acute disease, could be distinguished according to two distinct types. Their properties are as follows:

Type I.—Bacillus of the average size of B. coli communis. There is variation in length; almost none in thickness. The individuals are usually separate; sometimes they are united in pairs, but only very rarely do they occur as filaments. The ends are slightly rounded. The bacillus shows moderate motility; Gram's stain is negative.

Growth takes place upon all culture media at the room temperature, but better in the thermostat. Gelatin is not liquefied. The colonies resemble those of B. typhosus, being more nearly like them when first isolated from the dejecta than after a period of cultivation outside the body. After many months of such saprophytic growth the colonies become thicker, exhibit a moist surface and are less translucent. The strokes upon agar-slants show a similar alteration. At first the growth extends but little laterally, but later on it becomes 2 to 3 mm. in width, and generally shows distinct indentations at the edges. Upon gelatin the colonies are more delicate; the stab extends along the line of puncture only, spreading very little at the surface of the medium.

On potato, growth takes place along the line of inoculation and spreads beyond. After some days it is a little elevated and of a pale-brown tint. On unfavorable potatoes the growth is slight, moist and membranous, resembling, except for the greater amounts of moisture, that of B. typhosus when typical.

Sugars—glucose, lactose, and saccharose—are not fermented gaseously. In glucose media a moderate acid production takes place.

Bouillon is clouded diffusely and a sediment forms. There is no production of a pellicle.

Litmus-milk assumes, after 24 to 72 hours, a faint lilac tinge. After the lapse of from 6 to 8 days alkali begins to be produced, which increases in amount until the litmus is rendered deep blue in color. No coagulation of the milk ensues.

Indol is not always formed. Even in sugar-free bouillon it may fail to appear, or it may be produced in small quantities only.

Suitable cultures of this organism, when tested for the agglutination reaction with the blood-serum of persons suffering from dysentery—the host of another individual—give, in many cases, a positive result.

The bacillus is pathogenic for the ordinary laboratory animals. It is abundant in the acute cases in which it may be the predominating organism; it becomes more difficult to find as the cases progress towards recovery or chronicity. In the ordinary chronic dysentery of Manila, in which amebæ are commonly encountered, it was not found. It can be cultivated from the dejecta during life, and the intestinal contents, mucous membrane and mesenteric glands in fatal cases.

Type II.—Bacilli which are present in all instances. In the acute cases they may not predominate, being less numerous than the members of Type I. In all others it is the predominating bacterium. The properties vary somewhat, but agree well with those of the group B. coli communis. The main variations relate to extent and rapidity of growth upon the several culture media, the rapidity with which litmus-milk is reddened and coagulated, and the amount of indol produced. The sugars are broken up with the formation of gas. The morphology is also similar to that of B. coli; some specimens are motile at the end of 24 hours; in others motility was not demonstrated.

In agglutination tests the results varied according as the blood of the host or of another individual was employed. With that of the host there was frequently a reaction in low dilutions; with that of another person the reaction was rarely and very inconstantly obtained. The pathogenicity was not tested extensively

The practical operation of separating the several kinds of bacilli which grew in the plates was to inoculate glucose-agar stab-tubes from the different colonies. In those tubes which, after 24 hours at 37° C., showed no gas, the organisms were likely to conform to Type I.

Before proceeding to the assumption that this organism was concerned with the production of the intestinal lesions of dysentery occurring in Manila, it was necessary to establish its absence from the stools of healthy persons and of those suffering from other diseases. Strong presumptive evidence of its being an unusual inhabitant of the intestine of man may be gathered from the facts already known concerning the ordinary intestinal flora. But as such observations would not suffice for a new region and under new conditions, the organism was searched for in other persons who had been in close association with those suffering from dysentery and also in inhabitants of other parts of the Island of Luzon. The organism was not demonstrated in healthy dejecta or in evacuations of persons (native Filipinos) suffering from beriberi. A further argument in favor of its restricted distribu-

tion is furnished by its absence from cases of chronic dysentery or the marked reduction in the numbers present.

Pathogenicity.—The pathogenicity of the bacillus Type I was studied, soon after its isolation, upon mice and monkeys in Manila, and upon various animals in this country with cultures brought from the Philippines.

Monkeys.—Subcutaneous inoculation gives rise to a swelling from which the animal suffers no inconvenience and quickly recovers. Monkeys which were given croton oil and, after purging had been established, 10 cc. of a bouillon culture through a stomach-tube, soon recovered from the effects of the purge, and no further results could be noted.

Mice are susceptible to subcutaneous and intraperitoneal inoculations. Death takes place in from 24 to 48 hours—rarely after several days—the reaction varying according to the dose and the mode of inoculation. The site of puncture shows edema and, in the case of injections made beneath the skin, a hemorrhagic exudate. Inoculation into the peritoneal cavity gives rise to a variable amount of faintly turbid exudate and small white flakes of leucocytes; the pleura contains an excess of clear fluid, which is often present also in the pericardium; the serous vessels are injected and small hemorrhages may occur, more especially in the subcutaneous tissues. The superficial lymphatic glands are swollen and congested or hemorrhagic; the spleen is enlarged, the kidneys and adrenal glands are congested; the lungs show a marked congestion and the intestines contain an excess of glutinous contents. Coverslips from the peritoneal and pleural exudates show bacilli, often in large numbers, and polymorphonuclear leucocytes. These cells frequently show engulfed bacilli. Cultures prove a general invasion of bacilli with relatively smaller numbers of organisms in the spleen and heart's blood.

Guinea-pigs react in much the same way as mice, larger doses being required to produce fatal results, while the bacilli show less tendency to invade the internal organs. Subcutaneous injections cause a local swelling consisting of pus-corpuscles, serum, and blood; the superficial lymph-glands become swollen, and an exudate appears in the peritoneal and more rarely in the pleural cavities. Intraperitoneal inoculations give more characteristic results. Death took place in from 1 to 6 days depending upon the source and amount of the culture. The inguinal and axillary lymphatic glands are enlarged and reddened; the peritoneal cavity may contain glutinous fluid and floating whitish flakes of pus-corpuscles, or with little fluid, there may be grayish-white solid exudates of considerable size over the liver, spleen, and intestines. The blood-vessels are injected, the small intestines are filled with a soft glutinous matter, ecchymoses occur in the mucosa of the intestines, and the Peyer's patches may be swollen and reddened. If death occurs late the swelling of the Peyer's patches may have disappeared and be represented by the "shaven-beard" appearance. The liver exhibits areas of coagulative necrosis of considerable size; the adrenals and the kidneys are congested. The pleural cavity frequently contains an excess of clear fluid and the lungs are mottled. The pericardial vessels are also injected and the sac contains an increased quantity of clear fluid. The distribution of the bacilli varies. With moderately virulent cultures they occur only in the local exudates in peritoneal and pleural cavities. In rare instances, indeed, they may disappear even from the abdominal cavity, be greatly reduced in numbers, absent from the internal organs and blood or occur there in very small numbers. This disappearance may have taken place when death has occurred as early as 24 hours after inoculation. Larger doses or intensified cultures give rise to a moderate invasion of the blood and organs. If the autopsy on these animals is delayed, especially in warm weather, an increase of bacilli in the blood rapidly takes place, so that erroneous results may be obtained. Within the local exudates the bacilli are surrounded by capsules and are often contained within polymorphonuclear leucocytes. The bacilli can also be cultivated from the fluid portions of the intestinal contents. The ingestion of cultures gives rise to no results unless the stomach-contents are first neutralized; in the latter case death may occur; the small intestine is hyperemic; the contents are hemorrhagic and mucoid and the bacilli can be cultivated from them.

The *rabbit* usually responds with a localized swelling at the site of the subcutaneous injection, from which the animal usually recovers. When the injection results fatally the local infiltration resembles that in the guinea-pig, being, however, more marked than in that animal.

Cats also succumb to subcutaneous injections. Feeding alone produces no result. If, however, croton oil be first administered and the culture be then introduced into the stomach, diarrhea sets in, the bacillus is recoverable from the dejections and death may result. In the last case the mucosa of the large intestine is hyperemic and secretes an excess of mucus. The *dog* may succumb to simple feeding of the cultures. In positive instances diarrhea sets in, the appetite is lost and death may take place in 5 or 6 days. The mucous membrane of the intestine is hyperemic; hemorrhages occur, and the cavity of the gut contains a great excess of mucus from which the bacillus may be recovered.

The dead cultures are also toxic. Certain results of the inoculations into guinea-pigs suggest that the fatal effects are due to a toxic agent rather than to an infection *per se*. Cultures killed by exposure to temperatures of 60° C. for from 15 to 20 minutes are still active. In the course of certain immunization experiments one of the goats of a series succumbed to inoculation with dead cultures. On November 22, 20 cc. of a bouillon culture, killed by heating to 60° C., were given under the skin of the shoulder. Considerable induration developed at the site of inoculation; diarrhea set in, from which the animal seemed to recover. On November 29, a second injection of 20 cc. of the culture was given; on the next morning the animal was dead. The *autopsy* showed edema over the site of inoculation. The nates were covered with thin, partly dried fecal matter. The mucous membrane of the gut was hyperemic and presented numerous punctiform hemorrhages.

Dead cultures injected into rabbits and guinea-pigs cause: (1) elevation of temperature; (2) symptoms of intoxication (especially in guinea-pigs) which may come on within two

or three hours after the injection; and (3) in rabbits, rapid recovery with a localized and decreasing swelling; in guinea-pigs, similar phenomena or death in a few hours or after 4 to 6 weeks. In the last instance the animals show great emaciation. In the case of those that have recovered from the immediate results of the injection agglutinating properties for the bacilli appear in the blood.

Has this Bacillus been Found in other Epidemics of Dysentery?—If the bacillus described is of significance in the etiology of dysentery it must occur with regularity in the disease. Whether or not it will be found to have the distribution that is necessary in order to establish this relationship, can only be determined from studies carried on in widely different places and in all forms of the disease. That the bacillus is identical with the organism obtained by Shiga in the epidemic of dysentery which prevailed in Japan, there can be no reasonable doubt. In morphological, cultural, and pathogenic characteristics the two organisms are indistinguishable.

Through the courtesy of Dr. J. H. Musser I have been enabled to study, bacteriologically and pathologically, a case of chronic dysentery contracted during the Spanish war in Porto Rico. The patient, a soldier, entered the hospital of the University of Pennsylvania in December, 1899. His dysentery dated back some months; the movements were frequently examined for amebæ with negative results. A brief abstract of the autopsy protocol is as follows:

The body is that of a greatly emaciated man about 35 years old. Dorsal decubitus. The peritoneal cavity contains a small amount of reddish fluid. The colon is thickened, and in the peritoneal surface, especially along the sigmoid flexure, shows dark points and lines of discoloration. The rectum and sigmoid flexure are contracted; the transverse colon, on the other hand, is dilated. The mucosa of the large gut is thickened throughout; in addition there are small, recent hemorrhages into its substance. There is no pronounced ulceration; the mucous membrane presents a granular aspect; there are superficial areas denuded of epithelium, and others, which are slate-colored and show dark pigmentation. The submucosa is not especially thickened except in the lower part of the gut, where there is much contraction. The mucous membrane of the transverse colon is edematous; the cecum is less affected than the colon, while the small intestine has entirely escaped. No pseudo-membrane is present except upon a small portion of the lower parts of the sigmoid flexure.

The bacteriological examination made from the contents of the hepatic and sigmoid flexures gave growths in which the two general types of bacilli already described were contained. The predominating form agreed with Type II (B. coli communis group); in addition, there were colonies of an organism which in morphological, cultural and pathogenic characters, and in the agglutination reaction, corresponded with the variety of bacilli represented by Type I. The histological appearances in this case differ from those in the acute disease and equally from those of the amebic variety. The changes are found more particularly in the mucosa and submucosa and represent, it would appear, a later stage in the course of the acute disease. Before describing the other changes it should be mentioned that a striking feature in the case is the congestion in the mucosa, submucosa and muscularis. Numerous large veins, distended with blood, occupy the field of the microscope. Whether these vessels are newly formed cannot be stated positively; but they certainly are many times larger than any preexisting vessels normally met with in the same situations. In a few places the surface of the mucosa shows a necrosis of the hyaline or coagulative variety, there being no appearances of exudative fibrin in these areas. These necroses do not include the entire thickness of the mucous membrane, but cap superficial foci. There can be no doubt that this tissue-death indicates an exacerbation of the acute disease, with which, indeed, the great congestion may be partially associated.

The chief and, as I take it, characteristic changes in this stage of the disease are proliferative in character. The mucous membrane is not markedly altered in volume. Its structure is, however, greatly modified. Very few glandular crypts remain. The membrane is represented by a mass of spindle and epithelioid cells together with a reticular and coarser intercellular network, enclosing the remains of the crypts of Lieberkühn. The submucosa, also, shows a new growth of tissue, in which, however, appear much more advanced changes. The submucosa is composed of dense, almost hyaline, and structureless tissue, taking a vivid eosin stain and enclosing foci of epithelioid cells. The hardening and distortion of the gut were, doubtless, caused by this new growth of tissue and its subsequent contraction. The dilated blood-vessels, mentioned above, occupy a prominent place in this coat. A variable number of lymphoid, plasma, and eosinophilic cells occur, especially about the veins.

The muscular coat is also the seat of a multiplication of connective-tissue cells, which is shown by the masses of epithelioid cells separated by muscle-fibers, as well as an increase in foci of the fibrous tissue.

Blood-pigment is present both in the muscular and the subperitoneal coat.

The careful bacteriological studies in Egyptian dysentery, made by Kruse and Pasquale, contain numerous references to typhoid-like bacteria. Critical examination shows the majority to belong to the groups of B. coli communis. The typhoid characteristics depend merely on cultural resemblances—most marked in growths on agar-agar. Fermentation and their effects upon milk eliminate the suspicion that they may be typhoid bacilli, or the organism obtained by Shiga in Tokyo, or by myself in Manila. Still other examples of bacilli, similar to and possibly identical with B. dysenteriæ (Shiga), have been found in dysentery, though they are not suspected of standing in any etiological relation to it. Pansini studied 4 cases of abscess of the liver, 3 of which followed dysentery. The bacilli, which were isolated, resembled B. typhosus—indeed, Pansini could not distinguish between the two series. Babes also, although only in a single instance, isolated such an organism from a case of dysentery.

Since the publications of Shiga's studies, Escherich and Celli have both attempted to show that the organisms obtained from their respective epidemics of dysentery are

identical with the B. dysenteriæ. In both cases they have proceeded upon the false assumption that Shiga's micro-organism was a variety of B. coli communis, whereas, in point of fact, it is much more nearly related in its cultural and physiological properties to B. typhosus.

The question naturally arises, In what ways does it differ from B. typhosus? Comparison of the Eberth-Gaffky and Shiga bacilli show the criteria of difference to be by no means numerous. The main features, however, are as follows: The latter shows less marked motility when first isolated and a tendency to lose motility rapidly in artificial cultivations; it displays a more uniform generation of indol; after a brief preliminary acid production in milk it gives rise to a gradually increasing alkalinization; it is inactive to blood-serum from typhoid cases; but reacts with serum from dysenteric cases to which B. typhosus does not respond.

The Agglutination Test.—While the absolute value of this test in determining the specificity of bacteria may be open to doubt, its use in differentiation is now unquestioned. Undoubtedly there are limits to its usefulness, and experience (gained especially in typhoid fever) has shown that the changes upon which the property of the blood-serum depends for its evolution in certain instances may fail to take place. The tests in the case of the bacillus isolated in Manila were made at the time with blood obtained from acute and chronic cases of dysentery, occurring there and in the surrounding country. For carrying out the tests the blood was obtained in capillary tubes from the lobe of the ear of the living, and in larger quantities directly from the cavities of the heart by means of sterilized pipettes from the fatal cases of dysentery. The tests were made under the microscope and by growing the organisms in mixtures of bouillon and blood-serum. After our return to this country, the blood-serum from the case of Porto-Rican dysentery was employed and gave positive results. Through the courtesy of Assistant Surgeon Craig, stationed at the Presidio at San Francisco, I obtained capillary tubes filled with blood taken from convalescents and other soldiers suffering from chronic dysentery acquired in the Philippines. The present status of the agglutination reaction may be summed up as follows:

Positive results were obtained with cases definitely known to have been infected with the microorganism in question. The results obtained from the blood derived from chronic dysentery were more variable. Dr. Osler has written me of his experience. In several cases of amebic dysentery which have come under his charge in the Johns Hopkins Hospital, the blood-serum failed to produce the reaction with the bacillus obtained in Manila; in one case of the Porto-Rican disease a positive reaction was given.

The above results tend to emphasize the distinction of types of dysentery occurring in the tropics. They further tend to confirm the possibility that the acute dysenteries are caused by B. dysenteriæ. To what extent the organism is concerned with the production of chronic dysentery remains to be established. That we must recognize a chronic form of tropical dysentery that is not in its entire course associated with the presence of amebæ in large numbers, and that possesses totally different pathological lesions, is certain. I am inclined to the opinion that this type is not the commonest form of chronic tropical dysentery, and that it is less frequent than the amebic type. As it appears to be the form that gives a positive serum reaction with B. dysenteriæ, its extent and distribution may now be open to investigation.

Bearing directly upon these considerations are the results of Lieutenant Strong's studies continued after our departure from Manila. He writes: "After you left we had a large number of acute cases of dysentery. It seems certain that this form, which we have begun to speak of as *acute infectious dysentery*, is independent of amebæ. I have now records of 14 cases (not all were fatal) which I studied bacteriologically. From the stools in all of these, there has been obtained a bacillus which agrees with the organism obtained by you. I have also obtained the organisms from the mesenteric glands in three fatal cases. In one case of acute dysentery with secondary acute fibrinous peritonitis I obtained it from the exudate. The agglutination reaction is not invariable. Amebæ were never demonstrable in any of these 14 cases. On the other hand, in every case with certain anatomical lesions we always find the amebæ. In some cases of dysentery in which the amebæ were absent and the bacilli present, that have lasted four to five weeks (one case lasted nearly two months) and then resulted fatally, we see a continuation of the same process that is observed in the acute fatal cases. The lesions are those of necroses of the mucous membrane and induration of the gut."

Protective Inoculation and Serum Therapy.—It is not unreasonable to hope that with the discovery of the specific cause of dysentery, particularly if it proves to be a bacterium capable of being artificially cultivated, means will be found by which protective inoculation may be carried out with effect and safety. The fundamental conditions underlying such immunization are now fairly established, and two general methods of accomplishing such results are open to investigation. In the first place, an active immunization may be achieved through the use of cultures of a determined grade of activity; in the second the serum of animals may be employed either as a therapeutic agent or to provide a passive immunity.

It has been found possible, through the use of cultures destroyed by heat or the addition of chemicals (tricresol), to protect small animals from subsequent inoculations with virulent bacilli. Larger animals, such as the goat, when treated first with the dead and afterwards with the living cultures, develop a gradually increasing resistance to the inoculations; their blood-serum assumes highly agglutinating qualities for the bacillus, and coincidentally acquires protective and healing properties. My own experiments relating to this topic have been carried out on small animals only. Shiga, has, however, been able to test the serum upon human cases. Dr. Eldridge[2] in his report gives the following figures: Up to November 1, 1899, Shiga had treated with the serums in 1898 in Laboratory Hospital, 65 cases, death-rate 9 per cent;

[2] Public Health Reports, Vol. XV, No. I.

in 1899 in Laboratory Hospital, 91 cases, death-rate 8 per cent; in 1899 in Hirowo Hospital, 110 cases, death-rate 12 per cent. During the same period of 1899 there were under ordinary treatment at Tokyo: at Honjo Hospital, 166 cases, death-rate 37.9 per cent; at Hirowo Hospital, 53 cases, death-rate 37.7 per cent; at Komogome Hospital, 398 cases, death-rate 34.6 per cent; in private houses, 1119 cases, death-rate 28.5 per cent.

I should, however, expect greater benefit from a species of vaccination, especially to those exposed to the endemic or endemo-epidemic dysentery of the tropics. The encouraging results of the injections of the dead bacilli of Asiatic cholera and typhoid fever render justifiable the use of a similar procedure in persons exposed to dysentery. The practical details of such inoculations will, of course, be established only after trials, preferably upon human beings who are anxious to submit to this method of treatment. I have found it possible to prepare cultures which after being killed possess a definite degree of toxicity for guinea-pigs. The only example of an experiment upon man yet available is that performed by Shiga, who directed that about $\frac{1}{12}$ of an agar-culture, suspended in bouillon and killed by heat, should be injected into the subcutaneous tissues of his back. The immediate results of the injection were pain in the head, slight chill and fever, and local infiltration. After five or six days—the symptoms having in the interim entirely disappeared, except for some slight swelling—this area of infiltration increased and called for incision. The subcutaneous tissues were found thickened, indurated, and infiltrated with pus, which was sterile to cultures. The local lesion, similar to those in animals, was, it is thought, produced by the toxic substance contained within the dead bodies of the bacteria. Immediately after incision, all disagreeable symptoms subsided except the local infiltration, which disappeared gradually.

If this experiment can be taken as an index, the poison of B. dysenteriæ is more active than the analogous substance contained in the bodies of the typhoid and Asiatic cholera organisms. This objection, if true, could be eliminated by dosage, or, if necessary, by combining the vaccine with immune-serum, as has recently been recommended by the German Plague commission in carrying out the inoculations with the Plague bacilli. Shiga's blood-serum, 10 days after the injection, showed active agglutination of the bacilli.

An interesting, if somewhat disagreeable accident, was experienced by one of the laboratory assistants in Baltimore. In studying the acid production of the Manila bacillus a small quantity of fluid culture was aspirated into the mouth. The culture was expectorated and the mouth rinsed with a weak carbolic-acid solution. Notwithstanding this precaution a severe diarrhea, with bloody and mucous stools, pain and tenesmus developed within 48 hours. I was in Philadelphia at the time and the scientific ardor of the patient was so greatly depressed as a result of his discomfort and suffering that cultures were not made from the dejections, nor was I notified of the accident until several weeks afterwards.

Very little remains for me to say at this time. It is only natural to ask whether the foregoing considerations justify a belief in a specific organism of dysentery. My own sense is against that belief, although it must be conceded that the varieties of the disease are fewer than the clinical and pathological-anatomical conceptions of the time would lead one to suppose. Excluding the sporadic cases, which need a much closer bacteriological study than has been yet accorded to them, it is entirely possible that two specific organisms may be responsible for the epidemic and endemic diseases *per se*. I think that I have shown that tropical dysentery consists of a bacillary and an amebic form, separable in their early and their later stages by their clinical histories, their etiology and pathological anatomy. It is important to know whether the epidemic disease is more uniform in its causation and pathological anatomy. The studies of the Japanese disease by Shiga are highly suggestive of this interpretation, but additional observations will be required before we can accept as final his conclusions.

A CONTRIBUTION TO THE STUDY OF THE ANATOMY AND PHYSIOLOGY OF THE PROSTATE GLAND, AND A FEW OBSERVATIONS ON THE PHENOMENON OF EJACULATION.

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It is not the purpose of this paper to go into the complete anatomy and physiology of the prostate gland; but to discuss some points, in relation to its finer histological structure, which have not hitherto been clearly elucidated.

Review of the literature.—In the literature many papers have appeared from time to time, but the ones that show exact investigation are strikingly sparse. In most of the various works on histological anatomy the descriptions are short, superficial, and in not a few inaccurate. By Henle,[33] Kölliker,[34] Sappey,[41] and L. Testut,[42] much more detailed, and better accounts, are given.

Home, [35] in 1806, announced the discovery of a third lobe, posteriorly, between the two lateral ones. For many years this view was accepted by all the English anatomists, but denied by the French. Later, Thompson,[40] in 1857, made some careful examinations of a large number of cadavers; and

arrived at the conclusion that it is only occasionally present, and does not deserve the name of a third lobe. Recently, these observations have been confirmed by Griffiths.

Pettigrew,[26] Bell, Sabatier,[39] and Shaw [42] have described the gross structure and muscular arrangement, with varying degrees of exactness; but, unfortunately, their accounts by no means agree.

The embryology has been studied by Tourneux[30] and Mihálcovicz;[30] and the evolution, in dog and man, by Regnauld.[37]

In Rüdinger's[38] monograph very good observations are given on the caput gallinaceum and prostatic glandular substance, but the stroma is rather superficially treated.

Stilling[46] has made a careful study of the cellular elements in rabbits and man, with reference to the origin of the concretions. He observed the organ, before and after coitus, and at different seasons of the year.

Langerhans[25] gave the best account, up to that time (1874), of the glandular tissue in man.

Svetlin[47] made a series of investigations, in order to establish definitely the exact number of ducts. He found after the examination of numerous adult glands that the number varied between fifteen and thirty-two.

The work of Griffiths is well known, and is probably the most practical that has been done on the gland. He has busied himself more especially with the changes that occur at different seasons, at different ages, and after various operations.

In the writings of Oudemans[44] and Disselhorst,[8] very good general descriptions of the gland are found; but the scope of the work was too broad to permit a minute histological investigation.

The opinions regarding the organ as a gland are very diverse. Thus Ellis[10] says its chief office is muscular, and he thinks the term "gland" should be abolished.

Handfield Jones[16] is of the opinion that it should be looked on as an aggregation of scattered tubules, rather than a gland proper.

Harrison[17] acknowledges the existence of the glandular substance, but holds practically the same view as Ellis.

Henle, Kölliker, and Sappey give prominence to its glandular nature; while Stöhr,[45] Orth,[33] and many others state that the organ is largely muscular.

Griffiths affirms that its chief function is glandular, and that it is entirely connected with the sexual organs.

Material used. The research was made on specimens obtained from man, the dog, cat, swine, mole, hedgehog, bull and hamster. Most of the work was done on the dog, as human material could not be obtained of sufficient freshness to permit of a study of the finer histology. Comparison has convinced me that no great difference exists between them. In man, the glands were examined in the adult, new-born and embryo; in the dog, in all stages of development; in the cat, full-grown and new-born; in swine, full-grown, castrated, and embryo; in the hedgehog, full-grown, half-grown, and embryo; in the bull, mole and hamster only full-grown animals were utilized.

Method and technique.—The glands of the animals were taken immediately after death, and fixed in the following fluids: Zenker's, Herman's, Flemming's, van Gehuchten's; alcohol in various strengths; formalin 5% and 10%; sublimate 1%, 5% and concentrated; osmic acid, both by injection and maceration; diverse combinations of picric acid, formalin, and alcohol; acetic acid, sublimate, and picric acid; sublimate and osmic acid; chromic acid; and lastly a mixture of 3% pot. bichrom. and 5% acetic acid.

The best cell fixation was obtained by Flemming's solution, 5% sublimate, and the mixture of 3% pot. bichrom. and 5% acetic acid. This last named gave a very beautiful cell outline and protoplasmic preservation, which equaled, in every respect, Flemming's. The best preservation of the muscle was obtained by 5% sublimate, Zenker's fluid, and 5% to 7% formalin; and the best connective tissue in alcohol, 5% and concen. sublimate, and a mixture of alcohol and sublimate.

The glands were all imbedded in paraffin, and cut in varying degrees of thinness; from 2 to 20 mm. For a study of the cells, 2 to 4; for connective tissue by the digestion method, 4 to 6; for elastic tissue, 12 to 20; for muscle, 18 to 20.

Transverse and longitudinal serial sections were made in the new-born child, in the half-grown, and new-born dog. Transverse, in the adult cat, full-grown, half-grown and embryo hedgehog, and embryo swine.

All the approved staining agents were tried, with varying degrees of success. The one found to give the clearest definition of nucleus and protoplasm was Heidenhain's iron-hæmatoxylin, alone, and counterstained with a 1% aqueous solution of rubin. In several instances a very beautiful nucleus was obtained by gentian violet, after osmium fixation; but no satisfactory result could be had with thionin.

For the muscle Van Gieson's picrofuchsin method was employed. Many consider this a very delusive and unsatisfactory stain, but I found quite the contrary to be true. Tissues fixed in Zenker's, alcohol, formalin, and sublimate, stain well; osmium preparations and specimens that have lain for a long time in chrome solutions take it poorly. After a method of Dr. Hoehl, I usually applied an aqueous solution, of 1% iod. kal. and 0.5% iodine, previous to staining. This is a very important addition, and enables one to get a good result, where the picrofuchsin would hardly tinge the section. The connective tissue showed with greatest distinctness in specimens fixed in a mixture of picric acid, formalin and alcohol. The staining will be discussed under the connective tissue.

The work was done in the laboratory of Prof. Dr. Spalteholz; for whose great kindness and efficient help let me here express my heartiest and most sincere thanks. Also to Professor His for materials given, and for the use of his microscopic sections. To Dr. Hoehl thanks are also due, for showing me the method of digestion, and for various points in staining.

The Position and Arrangement of the Muscular Elements.

On a superficial examination of the prostatic muscle, one sees a complicated network, of crossing and recrossing fibers, without apparent order or regularity; and it is only after a careful study of a number of serial sections, made from the gland in various stages of development, that a correct idea of their position and direction can be obtained. It must, therefore, be owing to this cause, that these various contradictory statements are found in the literature of this subject.

Review of the literature.—The internal sphincter of the bladder is spoken of by most anatomists as a thickening of the circular coat around the neck of that viscus. Others, Guthrie,[26] Taylor,[36] Bedford,[39] Hancock,[28] and lately Griffiths,[14] deny the existence of any such thickening, and assert that there is no real sphincter.

Pettigrew[36] recognized no directly circular fibers, and thought that they all ran in an oblique manner.

Into the caput gallinaceum, according to Morgagni[31] and Santorini,[40] were inserted muscular bundles, coming from the ureters. Chas. Bell[26] denied this, and claimed that they extended to the third lobe of the prostate. I shall attempt to show later on that both of these opinions are incorrect.

Ellis[19] regarded the prostate as essentially a muscular organ; consisting of circular and orbicular fibers, which are directly continuous with the bladder behind, and the urethra in front. According to him, it should be looked on as a specially developed portion of the circular muscle coat that envelopes the urethra behind the bulb or spongy portion.

Hodgson[18] described the gland thus: "The muscular structure, from the mucous membrane of the urethra to the capsule of the prostate, may be considered as a general muscle coat of the urethra; interspersed with glandular tissue, and somewhat altered in form to adapt it to its new condition."

Sabatier[29] was of the opinion that the prostatic muscle is made up entirely of circular fibers, which are not connected with the bladder. He described two circular layers; one belonging to the urethra, and the other to the prostate; the fibers of one being arranged excentrically to those of the other.

Pettigrew[36] enumerated seven layers which were continuous with those of the bladder. He considered the verumontanum to be mainly a muscular body which had an important muscular connection with the urethral orifices.

R. Harrison[17] (1886) asserted that the prostate is a largely muscular organ, whose chief function is to support the bladder. Later, in 1889, he cited a number of cases to show that the gland acted as a sphincter for the bladder. In one case, he explained incontinence of urine as being caused by a want of development of this gland. In the last edition of his book, in 1895, he says he has had no reason to change his opinion.

Kölliker[24] states that the gland is surrounded by a thick muscular capsule, from which septa pass into the substance of the organ. He describes a circular muscle extending more or less around the gland, and a second longitudinal, situated near the urethra. The arrangement about the single lobules is not given.

Griffiths[14] thinks that the prostatic muscle develops from the circular coat of the urethra, and is arranged in a circular manner about the lobules. It is only indirectly connected with the circular coat of the bladder.

Sappey,[41] Henle,[38] and L. Testut[35] say that the muscle is so disposed around the lobules, that they may be forcibly compressed.

In the majority of the books on histology there is no description given further than the assertion that the prostatic stroma is largely composed of muscle which extends from the muscular sheath surrounding the gland.

After having made a study of the gland in the before enumerated animals, I have arrived at conclusions which do not entirely agree with those previously set forth. In order to increase the clearness of the description, it is thought best to give the position and arrangement in the full-grown dog as seen in a series of transverse sections; beginning at the vesical neck, and going to the apex or urethral end.

First, there is met a bundle of thick muscle which is arranged principally in the circular direction; internally and externally to this is a thin longitudinal layer. As stated above, several anatomists deny the existence of this in man, but it was plainly to be seen in all the dogs examined. Hanging somewhat in relation, but not in immediate connection with the above sphincter, is a thick muscle whose fibers run longitudinally, circularly, and obliquely; the majority seem to take the last named course, and are disposed concentrically around the basal prostatic lobes. This muscle tapers, and becomes thinner towards the bladder; and in several instances there was a distinct fibrous septum between it and the vesical muscles. The bundles are smaller and much more compactly arranged than those of the bladder, and are on entirely different axes. The muscle encircles the entire urethra at this point; but the fibres are excentric to the urethral axis, thus being in strong contrast to the concentric circular coat. It is clear, therefore, that this muscle is not definitely connected with the urethra or bladder, but is associated entirely with the prostate. It is somewhat triangular in shape, and fills in the angle formed by the prostate and vesical neck. From it, projections are sent into and around the gland, in a complicated manner.

Anteriorly, a thick triangular-shaped projection lies in the middle, between the two halves; a second division, about one-half the size of the first, is placed outwards on the side of the gland. Posteriorly, it projects in a similar manner, connecting the two sides, and lying between the urethra and ejaculatory ducts; this is much thinner than the anterior portion.

The anterior division is pyramidal in shape, with the base on the surface, at which place it is 2 mm. in breadth; from base to apex 4 to 2 cm. It extends to near the middle of the gland, longitudinally, where it becomes very thin. The bundles of fibers run in various directions; the circular and oblique preponderate. It extends on both sides into the substance of the organ, on either side, penetrating between

and surrounding the lobules. The fibers diverge, passing from the side of one lobule to the opposite side of another, and so on, thus forming a figure-of-8 network around them. A dense thick sheath passes forward on the outside of the gland, and hugs the glandular substance very closely; this becomes gradually thinner, and disappears at the junction of the lateral and lower borders. On the surface of this sheath, there were seen numerous depressions which corresponded to spaces between the lobules; here the muscle undergoes very marked thickening, and gives off small septa which ramify in the substance of the gland.

As the middle is approached, the muscle becomes much thinner, more deeply situated, and the fibers assume a more longitudinal course. Now, to return to the posterior portion—vesical half—we find here the muscular bundles are not so compactly disposed, and their course can be more easily made out. In the center the fibers are distinctly circular, while immediately before and behind they are longitudinal. This mass lies between, and connects the hemispheres posteriorly; it extends on both sides into the substance and diverges around the lobules in the same way as in the anterior portion. Behind the above layer, and lying well out towards the periphery, there is a bundle of longitudinal fibers, which are entirely separate from the other layers; these increase in the urethral half, the bundles become larger and more aggregated, assuming a cord-like shape. As the end is approached, the two sides close in around this mass, and place it well up in the substance; still further on, the fibers assume an oblique course, and enter into the gland substance. In this region they become mixed with the longitudinal coat of the urethra, but are not a continuation of it, as is stated by many anatomists. The muscle is four or five times as thick as that of the urethra, and its fibers are arranged on a different axis. As we follow the sections we find, about the middle of the urethral half, a distinctly circular layer enclosing the urethra and several lobules of the gland. At this place there seemed to be a definite connection with the urethra, but in passing on they became entirely separate, and the urethral coat was seen to be distinct.

The urethral end, corresponding in man to the apex, is covered by a thick sheath of muscle, which lies in direct connection posteriorly with the above-described muscle, and slightly so with the anterior division. It extends deeply on the urethral surface, and on the upper surface is continuous with the sheath from the vesical end; on the lateral surface there is a break in continuity, which leaves a boat-shaped area over the base of one lobe, entirely uncovered with muscle. The gland is then, contrary to the generally accepted opinion, not completely surrounded by a sheath of muscle. From this layer, septa pass in between the lobules, and join those coming out from the vesical portion. I wish here to note especially the fact that the urethral end of the prostate stands well out from that canal, and that there is an entire separation of the smooth muscular elements.

On the upper and lateral surfaces, there is a thin longitudinal layer, which is continuous with the corresponding coat from the bladder. The bundles are sparsely scattered in the vesicorectal fascia, and partly within the capsule; they become thinner and sparser, and finally disappear towards the urethra. It is stated by Pettigrew, Sabatier, and others, that this muscle is directly continuous with the outer urethral coat; but such was not found to be the case, in any instance. Underneath this, on the vesical half, there is occasionally present a thin circular layer; it is a continuation of the coat of the bladder and extends only a short distance out on the upper and lateral surfaces.

The septa, as before mentioned, are offsets from the posterior and anterior muscle masses and external sheath. They are thickest towards the periphery, and extend between the lobules as strong muscular partitions; in the interior, they divide, and become thinner and thinner; so that towards the urethra they disappear entirely. The course and disposition, as seen in the transverse sections, are so complicated that no definite order can be discerned; but by a study of the different axes a beautiful arrangement is to be made out. The fibers run in a circular and longitudinal manner; the circular are thickest and ramify among the lobules in a figure-of-8 course, thus enclosing each in a circular sheath, but not encircling them in the way described by Griffiths. Internal to this is an oblique or longitudinal layer, which lies immediately next to the gland substance, and encases the lobule more or less completely. The fibers commence near the apex, course along the side, bend over the base and run down the opposite side. This coat is probably in connection with the coats of the other lobules, but this point could not be definitely decided. This inner coat is interspersed between the finer divisions of the alveoli; the outer is seen only around the lobule. Lusena has described the longitudinal fibers in man, but makes no mention of the circular ones.

The individual fibers lie very near the cellular layer, being separated only by capillary blood-vessels and a basement membrane. In other areas a sheath of connective tissue is also interposed. The muscle-cells are long and well developed, with large oval nuclei situated near the center. In many places they could be seen directly inserted into connective tissue.

Crossed striated muscle.—This was present only in the portion of the urethral half; it is derived from that part of the sphincter urethræ externus, called the sphincter vesicæ externus, or sphincter of Henle. This muscle is made up of an outer thick layer of circular fibers, and an inner very thin sheath of longitudinal ones; these form a bridge between the two sides of the gland and penetrate among two or three lobules. In the periphery it forms a partition consisting of four or five fibers; deeper, only a few cells are seen scattered in the smooth muscle. In the cat the mixture was so intimate that it appeared as if one were inserted into the other. The longitudinal fibers extend more deeply, and can be followed to the center of the gland; they are interspersed from the surface to near the urethra, in the anterior fibromuscular septum between the hemispheres.

Muscles of the prostatic urethra.—First, on the vesical end:

the longitudinal external coat of bladder is continued over the prostate, as has been described. The circular ends at vesical neck. The internal longitudinal fibers, anteriorly, end in the connective tissue around the beginning urethra; posteriorly, they are inserted into the uvula vesicæ. On section, this body projects prominently into the commencement of the urethra, and very much resembles the form of the caput gallinaceum. This probably accounts for the belief held by Morgagni[25] and Santorini[26] that muscular fibers extend from the urethral orifices, and are inserted into the caput gallinaceum. From the border of the uvula vesicæ to near the middle of the gland, very little muscle is seen around the urethra; towards the center, the posterior and lateral walls, there are seen irregularly distributed muscular elements, largely mixed with connective tissue. The fibers are small and short and very irregularly disposed, and cannot be said to form a definite coat. They are present in the base of the verumontanum, but not in a greater degree than in the other urethral folds. In the outer portion it is somewhat removed from the urethral mucous membrane, and lies posteriorly; further on, the muscle is connected with the longitudinal coat of the urethra. In the anterior and posterior portions of the urethral half, situated near the surface, there are present a few scattered bundles of longitudinal fibers which can be traced back into the urethra. The circular layer of urethra becomes more or less incorporated with the prostate, but there is no definite connection. In many glands the cellular elements encroach so near the urethra that nothing remains of the wall, other than a thin submucous connective-tissue coat.

To condense the foregoing into a few words, it can be said: That the vesical end of the prostate is surrounded by a thick muscle composed of longitudinal, circular, and oblique fibers, from which a large process projects anteriorly and posteriorly between the two glandular hemispheres; and a thick sheath is sent out on either side, which encases the fore, lateral, and dorsal surfaces. The posterior process extends to the urethral end, where it spreads out around the external surface in that region. From these muscular divisions, septa pass into the gland, and surround the lobes in a circular and longitudinal manner, giving to each lobule two distinct coats.

The muscle coats of the urethra and bladder are inserted into the prostate, and not continued through it, and the urethral coats in the prostatic portion are replaced to a considerable degree by prostatic substance.

Caput gallinaceum.—This organ is spoken of by Pettigrew as being essentially muscular. That it contains muscle is true, but that its bulk is muscle is erroneous. Around the glandular portion there is placed a moderately thick layer of circular fibers which serve to expel the secretion. The other muscular elements seen therein are derived from the ejaculatory ducts, which retain their muscular coats to very near the mouths. In the lower portions the sheaths are quite distinct, while higher they become blended.

New-born child and dog.—The general shapes of the prostates in these are different, but their histological structure is very similar. By a study of a series of sections, cut in the longitudinal direction, it is clearly to be seen that the longitudinal coat of the urethra diverges and runs in various directions between the lobules; while at the other end the circular coat of the bladder spreads out and ramifies in the gland, in a like manner, but in a different course.

These pass through the gland more or less at right angles to each other; the one circularly, the other longitudinally; thus giving every lobule two coats. In sections from the child, both could be easily observed; the inner being longitudinal and the outer circular. According to Griffiths[24] all the prostatic muscle is developed from the circular urethral coat; my examination has led me to a different conclusion.

In the hedgehog, mole and hamster, there is a separate circular coat for each lobule; and in the hedgehog a few longitudinal fibers are present. In the cat a similar disposition is present as in the dog. In swine the muscle of Wilson envelopes the whole gland.

It will be seen from the foregoing, that the prostatic muscle primarily develops from the muscular elements of bladder and urethra; but later it becomes entirely separate and exists as a definitely distinct muscle. It is composed of two sets of fibers, so disposed that each lobule may be individually compressed; and the gland as a whole, by the thick anterior and posterior layers. The whole muscular structure is arranged primarily, to compress the prostate, and not to act as a vesical sphincter, as has been supposed by many anatomists; notably by Harrison.[17] It is true that in the dog the gland must give the necessary constriction to the urethra, as the walls of the latter are very nearly replaced by it; but to say that it is a special sphincter is, I think, entirely erroneous.

First: On account of the anatomical reason given above.

Second: In the cat, and a number of other animals, the organ is situated at quite a distance from the bladder.

Third: In the hedgehog, mole, and animals of this class, it is above the urethra, and extends outwards and away from it.

Fourth: Horses and swine, which are commonly castrated in youth, do not suffer from incompetent bladders.

Fifth: In females the gland is absent, and no representative muscular structure is present; if its function were that of a sphincter, it would be found in them, even as in males.

Sixth: Men in whom there is want of development, or atrophy of the gland, do not suffer from incontinence of urine (Griffiths).

Seventh: If the muscle were connected in function with the bladder, it would not so completely atrophy after castration.

The strict prostatic nature of the muscle is also borne out by the evolution of the organ. I have noted in the very young glands that the lobules project out beyond the muscle, and the latter is later developed around them. This is also corroborated by Regnauld[27] and Mihálcovicz.[28] The latter writes: "Da die Prostatadrüsen früher zur Entwickelung kommen als die Musculatur, so scheint die mächtige Ent-

wickelung der letzteren eine secundäre Folgeder ersteren zu sein."

Amount of muscular tissue.—The muscular elements form in the dog about $\frac{1}{7}$ of the substance; in man, about $\frac{1}{4}$. Notwithstanding these facts, the organ is spoken of by Orth,[32] Stöhr,[33] and numerous others as being largely muscular. Thus Stöhr in his Histology says: "Die Prostata besteht zum kleineren Theile aus Drüsensubstanz, zum grösseren Theile aus glatten Muskelfasern." Ellis goes much further, and gives as his opinion that, as there is so little glandular substance, the propriety of calling the organ a gland is doubtful. These opinions are either the result of incomplete investigation or the examination of abnormal glands.

Ejaculatory ducts.—These retain their muscular walls to within close proximity of their openings on the crest of the caput gallinaceum. Henle[34] thought the muscle blended with that of the prostate; in some sections this appeared to be the case, but as the ducts were followed, it became evident that they were quite distinct. Finger speaks of a ring muscle around them, to act as a sphincter; this I did not observe; on the contrary, the walls got thinner as the mouth was approached.

Position and Arrangement of the Connective-tissue Elements.

The stroma is described in most articles on the prostate, as consisting largely of muscle; the connective tissue being supposed to play an unimportant rôle; and in the literature very little is said about it. Klein affirms that the stroma is essentially muscular; the connective tissue is present in very small amount and is situated in the capsule and finer glandular septa. Sappey, Henle, and L. Testut, all of whom give relatively lengthy descriptions, do not say anything exact in regard to it.

The glands of the adult, new-born, and embryo man and dog, in different stages of development, were examined.

This tissue was studied by the digestion method, and by staining with fuchsin, nigrosin, and Mallory's hæmatoxylin. Among the stains, the last named proved by far the best, and gave extremely clear and beautiful demonstrations of the finest fibers. My thanks are due to Dr. Caspari for specimens furnished.

The idea that the connective tissue is insignificant in amount is proved by the digestion method to be erroneous. It is shown to be relatively abundant, and will compare favorably with the reticulum of other secreting organs; it is amply sufficient to furnish the necessary support to the glandular structure, independent of the muscular tissue. The latter, no doubt, lends additional strength, but it is not placed in the gland for this purpose.

In the new-born and young animals, the connective tissue is in considerable quantity, forming about one-fourth of the organ, and is very rich in cells. As age advances, it becomes more fibrous, and is replaced to a certain extent by smooth muscle.

As found in the full-grown dog, it is arranged in the following way: On both the urethral and vesical ends there is situated, anteriorly and posteriorly, a thick wedge-shaped mass. Posteriorly, its shape is somewhat changed by the upward projection of the sulcus in this region. In the urethral half, similar, but slightly smaller, masses are seen. Toward the center of the prostate, longitudinally, the glandular substance very nearly approaches them, and the tissue becomes correspondingly thin. From these masses, thick, dense sheaths extend, and spread over the anterior, posterior, and lateral surfaces. Toward the median line, urethral and vesical ends, the gland is thick and contains a large proportion of muscle; while on the lower lateral surface it is thin, with no muscle. From this thick central portion, and from the anterior and posterior masses, broad and strong septa are sent into the substance and form partitions between the lobules; these in turn divide and ramify in the cellular tissue, forming a honey-comb network on which the cells rest. Into the alveolated spaces thus formed are yet finer projections which support a layer of cells and carry a capillary blood-vessel. Surrounding the urethra is a thick and dense mass, which cannot be differentiated from the stroma of that canal; from the lateral surface four to five similar septa, as was noted above, pass outward and join those coming from the exterior; these are broad near the urethra, and contain very little muscular tissue.

Lying immediately under the cells, and separating them from the capillary, is an extremely fine and delicate layer of apparently almost structureless tissue.

In these digested specimens, and those stained by Mallory's hæmatoxylin, it was very plainly visible. By the high power, it was seen to consist of extremely fine connective-tissue fibers. This forms the membrana propria, on which the cells directly rest; in several instances extremely fine elastic fibers were interspersed in it. The existence of a basement membrane has been denied by many; and others have held very diverse opinions in regard to it. Disselhorst affirms that the membrana propria, as seen with an oil immersion, consists of a structureless membrane. Regnauld, who has made a careful study of the gland in dogs, states that none is present. Stöhr affirms that it is very hard to demonstrate it in the human subject. Griffiths thinks it is composed of small epithelial cells. Stilling also says it is made up of small round cells. Langerhans is of the opinion that it cannot be differentiated from the remaining connective tissue. On account of the poorly preserved condition of the human tissue, I have not been able to demonstrate its presence; but, as it is found in all the other animals, a doubt can scarcely be entertained as to its existence in the human subject.

Connective-tissue cells, mast and plasma cells, and leucocytes were scattered throughout the connective tissue, being most numerous in the larger septa in close proximity to the cellular layer. In the active stage they are present in greater numbers, and in younger animals they predominate.

Incorporated in the stroma is a large quantity of muscular tissue, and running through it are myriads of small blood-vessels and capillaries.

In old age the connective-tissue elements become much in-

creased, by their own hyperplasia, and by a degeneration of the muscle. In castrated animals the gland is almost entirely transformed into connective tissue.

Distribution of Elastic Tissue.

The elastic tissue is spoken of by Romiti, Böhm and Davidoff,[3] Debierre,[7] Rauber, Henle, Quain, and others, as forming a part of the prostatic stroma, but no description is given. The only special work that I have found is by A. Antonini. He delineates a more or less concentric coat around the urethra, which he calls the fasci peri-ultrali; a thin crescentic layer under the mucous membrane of the verumontanum, the fasci otricolari; and those in the gland, fasci glandulari. Although we both worked on the dog, I have not found exactly the same arrangement.

Transverse and longitudinal sections were made from the dog, at different ages; and in man, both adult and new-born. Three methods of staining were employed; namely: Unna's orcein; Weigert's iron fuchsin; and Spalteholz's elastic-tissue stain. The last named proved by far the best and brought out the fibers with a clearness that could not be obtained by the others. A modification of Weigert's was employed, which very greatly improved the stain. It is as follows: Stain in the usual way for 45 minutes; wash carefully with water, then thoroughly with 96% alcohol; stain for one minute with a concentrated solution of picric acid in 96% alcohol; wash out surplus picric acid with common alcohol, then with absolute alcohol; clear in xylol and mount in the usual way. This counterstain gives a yellow background to the black fibers, thus greatly adding to their clearness, and bringing into view the finer ones which were invisible. A trial will convince one of the value of this addition.

First, lying just under the mucous membrane of the urethra, and completely surrounding that canal, is a sheath of longitudinal fibers. These are thicker in this region than on the other portions of the urethra, but are directly continuous with the urethra in front and the bladder behind. The outer fibers diverge into the substance of the gland, and form a figure-of-8 network around the prostatic ducts. This serves to give each a distinct sphincter, and offers an effectual method by which it may be kept closed. Interspersed in this network are other fibers, which are circularly disposed; these are most numerous on either side, and posteriorly; in front, only a few are present. From these circular and longitudinal sheaths above mentioned, fibers radiate into the larger septa, where there they form a rich plexiform network; and in turn send finer fibers into the connective-tissue framework, between the cells. With the oil immersion these fine fibers are seen to be in relatively large numbers, and in some places to extend directly into the membrana propria. They are disposed for the most part in a circular direction around the alveoli.

The capsule is stated by most authors to be very rich in elastic tissue, but in the dog I have found quite the contrary to be true. In the muscle, a relatively large quantity is present, but in the capsule proper, it is sparsely scattered. The anterior and posterior masses of connective tissue between the hemispheres is moderately rich in irregularly disposed fibers, which are in connection with those in the gland.

Caput gallinaceum.—In this organ there is a circular ring of fibers about the utricle, which extends downwards, and encircles the glandular substance more or less completely. Just underneath the mucous membrane, there is placed a crescentic layer of circular fibers; this is thinner than the former, and extends from base to apex. Encircling either ejaculatory duct is a denser circular sheath, which is partially blended with the above layers in the apex of the organ; but in the base it is entirely separate. In the base of the verumontanum, there is a projection upward of the longitudinal coat of the urethra; but not to a greater degree than on the lateral urethral folds. It appears, therefore, that in favorable sections the organ would present the appearance of containing a large quantity of the tissue, but in reality much of it belongs to the ejaculatory ducts and urethra.

In man the proportion in the organ itself is very much greater than in the dog; the coats above described are decidedly thicker and denser, and form over one-half of the entire stroma of the organ.

In the new-born baby there is a beautiful oval-shaped sheath surrounding the prostatic vesicle. Posteriorly, and at the sides of this, is a mass of longitudinal and circular fibers, which pass outward among the beginning ducts.

In castrated swine the elastic tissue almost entirely disappears. The same is most probably true of all animals.

Ejaculatory ducts.—These are encased in a dense coat which increases in thickness as the openings are approached; this is distinct and separate in its course through the prostate, from the elastic tissue belonging to that organ.

It should be remarked that, as the gland contains such a number of blood-vessels, some of the threads might have belonged to them. Care was taken in the examinations to exclude this error as far as possible.

In *puppies* the same arrangement was present as in the full-grown dog; the number, however, was much smaller, especially in the glandular portion.

In the *adult man* a similar disposition is seen to that in the dog; one difference is noted in the fact that the fibers in the glandular substance are more aggregated under the basement membrane, and probably a greater proportion lie in it.

In the membranous urethra the fibers are nearly all longitudinal; those at the neck of bladder are circular and oblique.

In the female urethra in this region, they are for the most part longitudinal.

Prostatic Glandular Substance.

The glandular elements, according to Mihálcovicz, are developed from the urogenital sinus; and the organ should be looked on as a highly organized urethral gland. This view I cannot accept; for it must be remembered that the Wolffian duct has its mouth immediately in this region; and it is therefore extremely difficult to differentiate the beginning ducts, whether they come from the one or the other. More-

over, the stroma, in part, originates from the genital cord, which surrounds the Wolffian duct; and the after-function proves beyond question, that it belongs to the generative, and not to the urinary organs. I think, therefore, it is most probable that the epithelium is an outgrowth of the Wolffian ducts; as are the testes, vas deferens and seminal vesicles.

The glandular substance is arranged in from 40 to 50 lobules, which are imbedded in a dense connective tissue, and surrounded by a beautifully placed muscular layer. It presents, in every sense, the character of a definite and compact gland, and is not, as asserted by Handfield Jones, "a number of scattered mucous tubules rather than a gland proper."

The lobules, as has been studied by Regnauld, and as I have observed them in the human embryo and new-born dog, project into the surrounding tissue as straight tubes. As the animal grows these give off branches from the sides, which divide again and again, until very complex lobules are formed. At first they are incorporated in muscle, but as they grow very much more rapidly than the latter, they pass beyond, and lie in the connective tissue. The muscle, later, extends itself and envelopes them. This is in striking contrast to the view held by Ellis, who affirms that "the glandular elements are only large urethral glands, which project among the urethral muscles." The tubules do not extend into the muscles, but, on the contrary, the muscles grow out into the gland.

The lobules are built on the alveolar type; are of a long conical shape, with the base toward the exterior, and the apex to the urethra; they measure across the base about 3 mm., and from base to apex one to one and a half cm. The base and sides are imbedded in connective tissue and muscle, as has been described. In the active stage, owing to a multiplication of their cellular elements, they are increased in size. From 5 to 7 lobules are placed in the longest longitudinal diameter, and 4 to 6 in the corresponding vertical; thus making from 25 to 30 lobules on either side.

The alveoli are relatively large, saccular in form, and have a diameter of 0.15 mm.; they permit a distention of twice or three times that size; toward the urethra they become smaller and less distensible. Five to seven are attached to a single duct; this empties into a larger, which in turn enters a still larger channel, until finally 3 to 5 main trunks are formed. These course toward the urethra, and unite, forming a common duct, about one to two mm. from the mucous membrane. In the posterior division of the gland the arrangement is different; there 4 to 6 lobules empty into the same duct, which penetrates the side of the verumontanum, and opens about 2 mm. behind the ejaculatory ducts.

The ducts, 30 to 40 in number in the dog, are about one mm. long and one-sixth mm. in diameter; they have no distinct coat of their own, but are surrounded by the dense connective tissue forming the urethral wall, and a special set of elastic fibers previously noted. They empty over the whole circumference of the prostatic urethra; the mouths are for the most part on a vertical plane with or behind the caput gallinaceum; only a few are situated in front. In man, the openings are mostly confined to the urethral floor, and number, according to Svetlin, from 15 to 32.

I have observed by a careful study of a number of serial sections, and by sticking fine objects into the mouths of the ducts, that they all open in such manner as to eject their secretion directly towards the mouth of the ejaculatory ducts. In the dog those that empty in front are directed backwards. This I consider extremely significant, and, so far as I know, it has not been previously observed.

Gland cells.—These have been studied by Rudinger and Langerhans in man; by Stilling in the rabbit, and by Griffiths in the active and passive stages of the hedgehog and mole. My description will be confined to the dog; with some observations, as obtained from the cat and hedgehog. Human tissue was also examined, but the preservation was not such as to warrant a study of the glandular substance. I am convinced, by many observations on animals, that unless this gland is fixed immediately after death the cells undergo very rapid changes; I think, therefore, that descriptions that have been made on the human gland do not represent, even approximately, the true condition.

The cells were fixed, and stained as previously stated. In the deeper parts, the cells rest on a distinct membrana propria, and are disposed in a single row; they are of the long columnar type, and vary in shape as they are closely or loosely packed together. In the former condition they assume very diverse shapes; polyhedral, very long columnar, pear-shaped, and sometimes triangular. These various forms were given as different types of cells by Langerhans, but I am sure that they were produced by pressure from the neighboring ones. No cell membrane is present; the free border was usually clear and distinct, but in some instances it was uneven and ragged; this condition was occasionally so exaggerated that the cell contents were directly continuous with the secretion in the alveolus. This was noted with different fixing agents, and it is a question whether it was the result of the fixation, or a bursting of the cell with discharge of contents; the material on the outside appeared identical with the cellular protoplasm. The protoplasmic border next to the adjoining cell was quite plain in specimens stained by Heidenhain's iron-hæmatoxylin, while by eosin and erythrocin it was not clear.

The protoplasm was in large amount; in the outer half, it was densely studded with deeply staining granules, between which it was lighter, but no definite spongioplastic structure could be made out; (this appeared identical with the secretion in the lumen). The inner half contained fewer granules, and among them there was to be seen a number of very delicate threads forming the spongioplastic network. In the immediate neighborhood of the nucleus, it was much clearer; and in some to such an extent, that it gave the appearance of a vacuole. Behind the nucleus—that is, between it and the basement membrane—the protoplasm was extremely scant, and in the very active stage none was discernible. In the same region, other cells were seen, which had probably dis-

charged their secretion; the protoplasm was less, and not so granular.

The nucleus is about the size of a red blood-corpuscle; it is situated at the attached end of the cell, and seems in some instances to rest directly on the membrana propria; it is very distinct, sharply circumscribed, strongly staining, and has on the outer border a definite rim. The substance presents one large, and several smaller, intensely staining bodies; they have a ragged outline and lie in an extremely delicate network of chromatin threads. In the beginning of the active stage, and in younger animals, the chromatin elements are plainer, and in not a few, definite karyokinetic figures could be noted.

In other portions of the lobule, the cells are low cuboidal, the protoplasm is small in amount, and nearly clear; the nucleus is proportionately smaller, and is situated in the middle of the cell. They present all the characteristics of a less active, or an almost inactive, stage of secretion. Where the alveoli are much distended, the cells are very much flattened; and in the hedgehog they form a thin, membrane-like lining. Golgi's method was used to demonstrate the cellular ducts, but none were discovered. Various stains were employed to show mucous cells, but all were unsuccessful.

Passing down toward the urethra, the cells assume a cuboidal shape; the protoplasm is less clear and not so granular. The nucleus is smaller, denser, and more deeply stained, and is placed near the center of the cell.

In the ducts the cells are much more flattened, the protoplasm forms only a small rim and is entirely clear; it surrounds a small, homogeneous, deeply stained nucleus. The lowest portion of the duct is lined by an ingrowth of urethral cells.

The secretion in the alveoli stains very deeply with eosin and picric acid; it contains small structureless flaky bodies, but no concretion.

In the half-grown dog, three to five layers of cells are present in all parts of the lobule. The under rows are flatly cuboidal, irregularly placed, and do not form definite layers; their nuclei are relatively large, and surrounded by a narrow rim of homogeneous protoplasm. The over layer is made up of larger cells, rather more columnar-shaped, with a medium-sized, clearly defined nucleus; the protoplasm in the outer half shows a beginning granular appearance.

In the new-born child and dog many layers of cells are seen; in fact the whole lumen is nearly full. They are closely packed, flatly cuboidal in shape and have a very irregular outline. The protoplasm is extremely small in amount, and, in some, almost invisible; the nuclei are proportionately large, and appear as homogeneous deeply stained bodies.

In a hedgehog, which was examined in the height of the active season, the alveoli were thrown into numerous folds by cellular projections into the lumen. The individual cells were long columnar-shaped, with an irregular, not definitely circumscribed free border. The protoplasm and nucleus presented the same characteristics as those already described in the dog; the former was perhaps more granular and more deeply staining. I was unable to study the gland in the winter season, and could not therefore observe the cells in the passive stage.

Adenoid Tissue in the Prostate Gland.

In the literature, no mention is made of the gland containing lymphoid tissue. In quite a number of prostates, bits of that tissue were scattered here and there throughout the substance. At first it was taken for round-cell infiltration, and not until toward the last of the work was its true nature determined. It is generally situated near the lateral surface. Two to three small nodes are usually together, with a rather thick layer of connective tissue between them. The nodes are surrounded by a thin sheath of fibers, which extend into the substance, and ramify among the peripheral cells; but do not penetrate far into the interior. In the specimens stained by Mallory, a very fine meshwork of extremely delicate fibers was discernible in the central parts. The cells are closely packed, and present the same appearance as lymphoid cells seen in other locations. Scattered in some of the nodes are minute channels, with extremely thin fibrous walls, and lined by endothelial cells; these are most probably lymph-vessels. Extending off into the prostatic substance are strands of connective-tissue, which form a kind of outside framework and support. The glandular prostatic tissue lies well up on the outside, being arranged as in other areas, and does not show any apparent connection with the lymph node.

Various methods were tried to inject the internal lymph spaces, but none proved satisfactory. With the superficial injections a few vessels near the periphery were filled—which did not look like blood-vessels—but were too few to give sufficient proof that they were lymph channels.

The Caput Gallinaceum.

This organ has been so well described by Henle and Rüdinger that it will be necessary to say only a few words in regard to it. Weber was the first to give an account of it; and in the works of many anatomists it bears his name; he thought it represented the uterus. Merkel, in 1848, promulgated the view that it had its homologue in the anterior portion of the vagina; which opinion has been accepted by Thiersch, Lilienfeld, Ratke, Mihálcovicz, and Tourneux.

The stroma, which consists of connective tissue, muscle and elastic tissue, has already been described. The glandular substance is situated near the apex; it is of an alveolated sacular form; has a moderately large lumen, and empties by a slit-like opening in the anterior portion of the crest. The cells are columnar shaped, arranged in a single row, and, in the active stage, show the same characteristics as the prostate, but to a less degree. The lumen is filled by a thin, slightly turbid alkaline secretion. After castration, as I have observed in the hog, the cells atrophy; and muscle and elastic fibers almost disappear.

It is asserted by many anatomists that this organ is functionless; but, considering the facts, that the glandular substance is made up of active epithelium, is surrounded by a thick muscle which serves to expel its secretion, and that

atrophy occurs after castration, I think it undoubtedly true that it furnishes a secretion which is necessary for the semen. The function of the hill will be fully discussed when speaking of ejaculation.

From the foregoing paper the following conclusions may be drawn:

First. The prostatic muscle is derived from the longitudinal coat of the urethra, and the circular layer of the bladder.

Second. Every lobule is surrounded by a circular and longitudinal coat, so arranged as to expel quickly and forcibly the secretion.

Third. The prostatic muscle of the full-grown animal is independent of both urethra and bladder, and is only indirectly in connection with either.

Fourth. The muscle is not so disposed as to compress the urethra, or to act as a sphincter to the bladder.

Fifth. The connective tissue is found in nearly the same amount as in other secreting organs; and is amply sufficient to give all the needed support to the gland, independent of the muscular elements.

Sixth. A membrana propria is present in all cases, and consists of very fine connective-tissue fibers. There is a sheath of longitudinal elastic fibers around the prostatic urethra, from which the outer fibers diverge around the prostatic ducts in a figure-of-8 manner, and thence onward into the glandular substance.

Seventh. Outside of the above named elastic coat is an incomplete circular set of similar fibers, which also pass into the glandular substance.

Eighth. In the gland substance a rich elastic mesh-work is seen lying under the cells, with a few extremely fine fibers in the membrana propria.

Ninth. The glandular substance forms about five-sixths of the organ.

Tenth. The cells are disposed in one layer; tall columnar shaped; have a large amount of protoplasm, and a well-defined nucleus. In the same lobule areas are present where the cells are entirely inactive.

Eleventh. Adenoid tissue is scattered at irregular intervals throughout the gland.

The Function of the Prostate.

The opinions of physiologists respecting the function of the prostatic gland have been very diverse and contradictory; some have gone so far as to assert that it has not sufficient glandular function to warrant the use of the term gland. Others claim, that as a gland, it fills a *very* important office.

Wagner was of the opinion that in some of the lower animals, it, in connection with the vesiculæ seminales, secreted a fluid, which was ejected into the vagina after the semen, and prevented the former from running out.

Ellis thought its main function was muscular, being that of expelling the semen into the forepart of the urethra; and that its glandular nature was very insignificant.

Harrison affirms that its chief rôle is to act as a support, and a sphincter to the bladder.

Handfield Jones asserted that "it should not be looked at as a gland proper, and that its part in generative function was not to add any essential element to the fecundating fluid, but merely to appropriate a viscid material involved, in which spermatozoa may be securely transported on their destined route."

Chapman states that the function is not known. Herman, Hensen, and others are of the opinion that the gland, in connection with other accessory glands, serves to give the motility to the spermatozoa.

Steinach, in a very careful and painstaking work, found that after extirpation of the seminal vesicles in rats, their fecundating property was very much decreased; and that with extirpation of both seminal vesicles and prostate, it was brought to nil.

Fürbringer gives a very interesting account of a patient suffering from spermatorrhea; the semen passed without sexual excitation contained nearly immotile organisms; while in that ejaculated during the sexual act, they were very lively and active. He thinks the change was due to a mixture of prostatic fluid; and concludes that the function of the organ is to give a secretion, that stimulates the movement of the animalcules.

In order to elucidate the subject more clearly, it will be necessary to say something respecting the motility of the spermatozoa. It is stated by nearly all anatomists that in the testis, the organisms are immotile or nearly so. Hammar found that in the epididymis, nearest the testicle where the semen was thick, there was no motion; but toward the beginning vas, owing to glandular secretion, the fluid became thinner, and a part of them were somewhat motile.

In the ejaculated semen, they are all motile; it appears, therefore, without doubt, that they must meet some substance on their outgoing, that influences their motility. In order to determine this, various experimentation has been done. Thus Kölliker found that they moved freely in lymph, blood-serum, weak alkaline solutions, &c.; while they were brought to a standstill by gums, dextrin, mineral salts, weak mineral acids, &c.

Herman and Gruenhagen affirm that the movement is lively in the secretion of the accessory sexual glands.

Steinach observed lively motion, in a mixture of normal salt solution, with semen taken directly from the testicle; but it came to a standstill in three hours. A second mixture was made with prostatic secretion; in this there was seen a very lively motility, which continued for twenty-one hours.

In order to throw still more light on this subject, a series of experiments was instituted, the results of which will be given in the following:

The dogs were killed by a blow on the head; the testes and prostate were removed and laid in a warm, moist oven. The microscopic examination was made on a Ranvier warm stage, which ranged between 37 and 38° Cel.; and every care was taken to make the work as nearly faultless as possible.

The semen was first examined alone, from the testicular

substance, globus major, globus minor, and vas deferens; secondly, with a mixture of prostatic juice; and thirdly, with normal salt solution.

We found: First. In the testicle itself there was no movement.

Second. In the globus major, no motility.

Third. In the globus minor slight movement of a few organisms, where the fluid was thin.

Fourth. In the vas deferens, slight motion in the portion where the liquid was thin; in the thick parts, which composed the largest bulk, there was no movement.

Fifth. In a mixture of prostatic juice and semen from the substance of the testicle, there was distinct, but not lively, motion.

Sixth. Semen out of the epididymis with prostate juice showed lively motility, which continued unabated for some time.

Seventh. Semen from the epididymis with normal salt solution gave lively movement, in the places where a mixture had occurred. In other areas where the liquid was thick, no motility was apparent. The same was also true of the prostatic mixture.

We explain the production of the immediate movement by a thinning of the fluid, and not by a distinct stimulating influence of the prostatic juice. The latter may also exist, but, from the following observations, we think the thinning is sufficient:

First. In the testicle and globus major the fluid was very thick, and no movement was seen.

Second. In the globus minor and vas def. a part of the fluid was thinned from the secretion of the epididymis; in this part alone was movement noted.

Third. After mixture with the prostatic juice motility was seen only where the semen was thin.

Fourth. After the addition of the salt solution the same was seen as with the prostatic secretion.

For the continued motility more is necessary than the mere thinning; for in the salt solution, all movement ceases after three hours; whereas, in the prostatic juice, it continues over 20 hours. (Steinach.)

From the above the following conclusions may safely be drawn:

First. That the immediate production of motility of the organisms is induced by a thinning of the testicular secretion with the prostatic juice.

Second. The continued movement is probably kept up by substances in the prostatic fluid, that either act as stimulants or as food for the organisms.

Third. Unless a homogeneous mixture is made, thick portions remain, where there is no movement.

Fourth. We take it, therefore, that, as the dog has no seminal vesicles, and the gland of Cowper is very insignificant, the function of furnishing a fluid, in which the spermatozoa can freely move, belongs entirely to the prostate gland. It then becomes apparent that the organ is almost as important as the organisms themselves.

Ejaculation.

The view was first promulgated by Weber, and has been accepted by nearly all anatomists since, that the *caput gallinaceum* became intensely congested during coitus, and prevented the back flow of semen into the bladder. In a perusal of the literature I have not found this contradicted. But in the course of my work on the prostate gland, I have become convinced that the idea is erroneous; the grounds for which are set forth in the following:

First. The verumontanum is not situated in the posterior portion of the prostatic urethra, but in the middle and anterior portions; so that, if the swelling was sufficient to block the urethra, it would obliterate the whole cavity.

Second. The caput gallinaceum is in the most capacious part of the prostatic urethra. It is not probable that an organ which was to act as an obstruction would be placed in a position which was most unfavorable for the performance of that function.

Third. The urethral fold covering the organ is as vascular as the others; but the substance of the organ proper is much less so; and in several cases, pointed out by Rüdinger, it was very deficient in blood-vessels. It is, therefore, not vascular enough to produce the necessary swelling to strongly obliterate the urethra at this point.

Fourth. From the crest it gradually slopes toward the membranous urethra, forming the crista urethralis anterior, and does not end more or less abruptly, as would be expected if it were intended to act as a valve. It is thus in a very poor mechanical condition to offer resistance, even if it were forcibly pressed against the anterior wall.

Fifth. The ejaculatory ducts empty on, or very near, the crest of the elevation; most of the prostatic ducts pour out their secretion opposite or behind it, so that if it were sufficiently enlarged to obliterate the urethra, it would entirely close both prostatic and ejaculatory ducts.

Sixth. The corpora spongiosa, in the anterior portion of the urethra, offer the same kind of resistance; and to nearly, if not altogether, the same degree as the verumontanum. The congestion is even greater in the penile portions, for the venous return is prevented by muscular contraction.

Seventh. In the hedgehog and cat the organ is placed considerably forward in the urethra; and between it and the bladder the urethra is narrow, and surrounded by a thick muscular coat, which offers all the necessary resistance.

Eighth. A cast taken of the distended urethra shows the organ pushed into the anterior portion and it is, relatively, a very insignificant elevation.

Ninth. An artificial erection was made by forcibly filling the blood-vessels of penis, prostate, and bladder. During this, a low melting paraffin was injected into the urethra; under very slight pressure it passed directly into the bladder. After the bladder was quite full, the pelvis was cooled, and laid in strong muriatic acid, until the flesh was removed. The cast thus obtained showed a moderately capacious prostatic urethra, with the verumontanum extending not more than half way to the anterior wall.

Tenth. During the highest point of an erection, micturition can be accomplished, although not with the same force as otherwise, but this fact proves conclusively that the urethra is not occluded. This point has been noted in the insane and I have personally observed it in other cases.

Eleventh. It may be argued that the prostatic muscle contracts, narrowing the urethra, and thus aiding in the occlusion of the canal. This cannot occur to a material degree, for the muscular arrangement is not such as to permit it.

The above is, I hope, sufficient to throw some doubt on a generally accepted theory, which I am convinced is erroneous.

Next will be considered the mixing of the semen and prostatic fluids, and the ejaculation of the same.

It has been shown, in what has been said of the prostatic function, that in the testes and epididymis, the vast majority of the spermatozoa were motionless, and that by a mixture of the semen with prostatic secretion they became distinctly motile.

It appears, therefore, absolutely essential for a mixture of the two fluids to occur; otherwise the organisms remain unable to move, and consequently not capable of producing fecundation. It was also noted that unless the mixture is perfectly homogeneous, large numbers of the organisms remain in thick portions of the fluid. As the semen is a thick, tenacious fluid, more or less mechanical means are necessary to produce a proper incorporation.

It can, therefore, be asserted that, first, a mixture of the two fluids must be brought about; and, second, that the union must be homogeneous.

We will now return to the anatomical arrangement, and see how this occurs.

The ejaculatory ducts always empty on the crest of the caput gallinaceum and the prostate by from 30 to 40 openings in the wall of the urethra. These facts have been noted by all anatomists, but no significance has been given to them. This arrangement, I shall attempt to show, is of the very highest importance.

The prostatic ducts, as I have seen by study of serial sections, and by sticking fine objects into the mouths of the ducts, all converge toward the caput gallinaceum, and are directed so as to eject their secretion toward the openings of the ejaculatory ducts. The two largest are situated just behind the mouths of the ejaculatory ducts, and throw their secretion in the same direction as the others. Thus, as the semen is being poured out, 30 to 40 streams of prostatic fluid are ejected into it. It now becomes apparent why the ejaculatory ducts open on this eminence; namely, to be in a position so that the ducts from the floor, sides, and roof, posterior and anterior, can reach it. We have in this way a most beautiful anatomical arrangement for forming a perfectly complete mixture of the two fluids.

I think, therefore, that the main function of the prominent eminence of the verumontanum is to afford a hill on which the ejaculatory ducts can empty.

If we revert to the muscle, we see that every lobule is surrounded by a relatively strong muscle; so disposed as to expel the lobular contents quickly and forcibly.

Thus, without physiological proof, we have an anatomical arrangement which proves the fact that it is necessary for a thorough mixture to be made.

It is now left to consider the expulsion of the fluid; before doing this it is necessary to glance at the muscular arrangements; namely, the sphincter of Henle, and the sphincter membranaceæ urethræ. The last named commences, we will say for convenience, at the outer portion of the urethral half of the prostate, and extends along the urethra, encircling the membranous and part of the bulbous divisions, and ends about the middle of the anterior half of penis. In man and dog, it is from 0.3 to 0.8 cm. in thickness; at the beginning it forms a bridge between the two sides of the gland, and is inserted into the connective tissue between the lobes. Immediately ventralwards it is thickened, and forms the so-called sphincter of Henle; which was supposed by him to act as sphincter to the bladder. This idea has been accepted by most anatomists, while others, notable among whom are Sappey, L. Testut, and Griffiths, have disputed it. The chief office of the remaining portion of the muscle is thought by quite a number of authors to be that of keeping the bulbous urethra closed, and accelerating the flow of urine. Henle, Frank-Martin, Hunter, Sappey, L. Testut, and Griffiths, were of the opinion that it was mainly connected with seminal organs, and aided largely in the expulsion of the semen.

First, in regard to the external sphincter of Henle, I am of the decided opinion that it does not act as a sphincter to the bladder; the grounds for which belief are set forth in the following:

First. The bladder is provided with a circular sphincter at its neck, which is amply sufficient to hold the urine.

Second. In the female no such muscle exists. If it were necessary as a sphincter, it would certainly be more needed by women, where the urethra is much shorter, and the bladder is dragged about by the uterus.

Third. As the prostate gland is between it and the bladder, urine would be permitted to enter the prostatic urethra, and would be stopped over the orifices of the prostatic and ejaculatory ducts.

Fourth. In the cat and some other animals, as first pointed out in this connection by Griffiths, it is removed quite a distance from the bladder, and could not act as a sphincter.

Fifth. In serial sections of the prostate and membranous urethra I found in every instance that the portion of the canal which was surrounded by that muscle was wide open, while the neck of bladder was closed.

The remaining portion of the muscle is no doubt concerned in the phenomenon of micturition, but that its chief work lies in that direction is very questionable. It was first pointed out by John Hunter that in castrated animals, this muscle becomes white, fibrous, and nearly functionless. Later, Griffiths confirmed these observations, and extended the research to other animals, which had a distinct rutting period.

In the castrated animals he found the muscle tough,

fibrous, and ligamentous; in the quiescent stage of the others, it was atrophied, contained a large amount of fibrous tissue, and had lost very largely its cross striation. I have observed the muscle in castrated hogs, and found it atrophied to a certain extent, but not to such a degree as seen by others.

Now, to return to the ejaculation; the semen is ejected forcibly into the urethra in the direction of the membranous (urethra) part. It does not pass backward into the bladder; first, because the manner by which it is ejected gives it a forward impulse; second, the neck of that viscus is closed by its own sphincter; and, third, the anterior part of the urethra dilates, and draws the fluid forward.

As the semen is being poured out, the longitudinal fibers of the sphincter urethræ contract and dilate the caudal half of the membranous, and a portion of the bulbous, urethra; this produces a large cavity, and the semen rushes in to fill it. When this is accomplished, the contraction extends to the end inserted into the prostate and draws the lobes together, thus compressing the prostatic urethra, and closing the orifices of the prostatic and ejaculatory ducts. The wave proceeds to the thick portion of muscle, immediately in front of the gland, and closes the urethra at this point; it will be remembered that here is the narrowest part of the canal, so that in this region a pressure that would hardly close the bulbous division, will strongly obliterate the whole canal; we see also that the muscle is thickened in this place. Here we have the sphincter that closes the urethra and prevents the semen from going back into the bladder. Therefore the so-called sphincter of Henle, which is in reality only a part of the sphincter membranaceæ urethræ, is not a sphincter to prevent the urine from going out of the bladder, but one to hinder the semen from going into it. The semen is now expelled from the urethra by the continuing contraction of the anterior part of the muscle, together with the bulbocavernosus, ischiobulbosus, and a part of the constrictor redi penis.

During later stages of the ejaculation, the prostatic and ejaculatory ducts remain closed, in the manner previously described. The muscular contraction in the vas deferens, seminal vesicles and prostate is probably kept up, thus putting the contents of the respective organs on extreme tension; so that at the moment of relaxation, the fluid rushes out and furnishes material for the second part of the ejaculation.

The above, on first sight, appears to be a long process composed of several stages, but this, in fact, is not the case. The semen runs into the anterior portion, directly after it enters the canal; the muscle then contracts, closing off the bladder, and expels it from the urethra.

It is impossible to subject this to experimental proof; and it is simply put forth as a probable theory, in the light of the anatomical arrangements.

NOTE.—I was not able to observe the gland in the quiescent stage; but examined it in castrated hogs, and found a moderately thick muscle which, macroscopically, did not appear fibrous; and on microscopic section the fibers were well developed and presented a distinct cross striation.

Although the muscle is chiefly connected with the sexual function, it is not to be expected that it will lose entirely its histological structure after castration, for the part it plays in micturition requires it to be active.

It is difficult to understand how a muscle, which, according to Griffiths, was "tough, fibrous, ligamentous, and had lost nearly all its cross striation," could be strong enough to act in obedience to the will, and check the flow of urine, during micturition. Such a function, he acknowledges, it possesses.

The conclusions that may be drawn from the above are the following:

First. The verumontanum does not prevent the entrance of semen into the bladder.

Second. The semen is prevented from passing backward into the bladder, by the contraction of the so-called sphincter of Henle.

Third. The prostatic ducts are so arranged that they eject their fluid directly into the outpouring testicular secretion, thus producing a homogeneous mixture.

Fourth. The longitudinal fibers of the sphincter membranaceæ urethræ dilate the outer half of the membranous, and a portion of the bulbous, urethra; and by this means draw the semen from the prostatic portion.

Fifth. During the last act of ejaculation, the orifices of prostatic and ejaculatory ducts are closed, and their respective fluids put on much tension; so that at the moment of relaxation, a sufficient quantity of semen is poured in for the next emission.

Sixth. The sphincter membranaceæ urethræ aids, not only in carrying the semen along the urethra, but helps very materially in expelling it.

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A PIN IMBEDDED IN THE RECTUM.

By Otto G. Ramsay, M. D.,

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Foreign bodies are not uncommonly found located in different portions of the alimentary canal, and such small objects as pins, tacks or fish-bones, which are easily swallowed, and which from their size and shape pass easily through the ileocæcal valve, are not infrequently removed from the rectum. The following case of foreign body is of interest, not so much from its rarity then, but because of the peculiar way in which the pin was imbedded in the rectal wall.

The patient, E. W., widowed, age 55, came to me on Dec. 2, 1899, complaining of a feeling of pressure in the rectum, of general malaise, and of having passed blood with the stool on several occasions. On careful questioning the patient stated that she had been troubled with some vague abdominal discomfort for about 5 years, though she did not attach any importance to her symptoms, as they were but slight. I do not believe they had any connection with the passage of the foreign body through the intestinal canal. Two weeks before coming to me she was suddenly seized with sharp pain in the rectum, and constant rectal tenesmus. This pain was stabbing in character, most severe when she exercised, or when the bowels were moved, but always present as a dull ache even when she remained perfectly quiet. She had seen traces of blood in the stools on several occasions, and had suffered one slight hemorrhage from the bowel.

Examination revealed normal external and internal genital organs. On introducing the finger into the rectum a wire-like body was immediately felt, projecting across its lumen, about 1½ cm. within the anus. This, on more careful examination, proved to be a pin with its head buried to the depth of 5 mm. in the lateral wall of the gut, the point being free and impinging against the opposite wall. The rectal mucosa in this area was somewhat thickened from the constant irritation of the sharp point, and a free sanguino-purulent discharge covered the finger when it was withdrawn from the bowel. Slight induration of the rectal wall around the point of penetration of the pinhead was felt, but no signs of abscess formation could be made out.

The pin was easily removed by introducing a pair of forceps into the rectum guided by the finger, seizing the point to prevent its wounding the mucosa, and dragging the head from its bed in the rectal wall. The whole operation required but a few moments for its completion, and caused but little pain. It was not necessary either to use an anesthetic or to dilate the sphincter, as the foreign body was so close to the anus, and though some little pain was caused by the manipulation, it was not by any means unbearable.

The after-treatment consisted in frequent irrigations of the rectum with warm normal salt solution, and regulation of the bowel movements. This treatment gave complete relief to all the symptoms, and an examination two weeks later revealed a normal condition of the tissues.

A case of this kind is interesting chiefly from the difficulty in determining how the pin could have reached this position, and afterward have become imbedded in such a way in the rectal wall.

Four methods may be imagined by which foreign bodies can enter the rectum. First, they may be swallowed and traverse the intestinal tract to the rectum; second, they may be introduced into the rectum through the anus; third, they may enter the rectum by ulceration through its wall, from surrounding tissues or organs; and fourth, they may be formed in the intestine (enteroliths).

In my case the third avenue of entrance can almost certainly be thrown out of consideration, as the patient was perfectly certain that she had never stuck a pin into herself; and if a pin had penetrated any portion of the body deeply enough to remain imbedded in the tissues, she would certainly have been cognizant of this fact.

This leaves but two methods by which the pin might have reached the rectum, and it is more probable that she swallowed it, rather than introduced it through the anus.

That it is not an infrequent occurrence for pins to reach the intestinal tract in this way is shown in an article by J. F. Mitchell, appearing in the Johns Hopkins Bulletin of Jan.-Feb.-March, 1899, entitled "The Presence of Foreign Bodies in the Vermiform Appendix, with especial reference to Pointed Bodies," in which he describes a number of cases of pins and other like bodies in the appendix. Since the appearance of this article, several like cases have been reported, and in all of them the pin was evidently swallowed, as it would be impossible for it to reach the appendix in any other way.

The same fact is proved by the number of other foreign bodies found in the rectum—fish-bones for instance, which are certainly swallowed. Goodsall ("Notes on 20 Cases of Foreign Bodies in the Rectum," St. Bartholomew's Hospital Reports, Vol. XXIII, 1887, p. 71) reports twenty cases which he saw personally; in this number a fish or other bone was present nineteen times; a pin, once.

It is easy to conceive how a pin might be swallowed when the habit so frequently indulged in by women, of holding pins in the mouth while fitting a dress, is considered, and the ease with which it slips down is evidenced by numerous examples of the so-called "human ostriches," exhibiting in circus and vaudeville performances, who swallow with apparent ease nails, hairpins, chains, glass and other comparatively large bodies. A pin might also fall from the dress into the food and be swallowed without consciousness of the fact, and this is probably the way in which my patient became possessed of her foreign body.

From a consideration of the general character of foreign bodies removed from the rectum, with the history of how they reached this organ, we may conclude that the bodies introduced into the rectum through the anus are commonly of large caliber, and usually not sharp, while those entering the rectum from above are apt to be small and elongate in shape. This rule points in my case to the entrance through the mouth, rather than to its introduction through the anus.

How the head of the pin became imbedded in the bowel wall while the point remained free is a more difficult question to answer. It seems probable that, as the pin was forced down by the peristaltic movement of the bowel, imbedded in fecal matter, the head in some manner became engaged in one of the rectal pouches. We might suppose, then, that the pin would lie against the rectal wall, the head downward and the shaft extending upward parallel with the intestinal lumen. Sooner or later ulceration would occur, and the head become buried in the mucous membrane; after this had occurred the passage of a hard fecal mass, or a violent peristaltic contraction, would force the point downward across the lumen of the bowel, when the acute symptoms would begin.

That the point of the pin, instead of the head, did not become imbedded in the rectal wall seems to be only a matter of chance; if this had occurred, it is reasonable to suppose it would have penetrated the tissues more deeply, and a perirectal abscess would have resulted. Goodsall (*l. c.*) speaks of a case in which an abscess formed around the pin, giving rise to a blind internal fistula. In this case the head of the pin had penetrated the rectal wall, as on operation the pin was found projecting into the rectal lumen through the opening of the fistula.

It is not difficult to conceive why, after passing through the whole intestinal canal safely, probably imbedded in a mass of fecal material, it should have caught so close to the anus, as it can be explained by the narrowness of the anal opening, when compared to the rest of the intestine. Goodsall concludes from the study of his twenty cases "that the site of the puncture is within the last inch or three-quarters of an inch of the rectum." This situation may be explained in all of the cases by a transverse position of the foreign body and the comparative narrowness of the anal opening.

The length of time required by such a body to traverse the intestinal canal cannot be determined from the history given by my patient. Goodsall, from studying the previous histories of his cases, states that the time varies between one and nine days, and from the comparatively clean appearance of the pin in my case, probably about the same amount of time was required.

The immediate treatment was perfectly simple, consisting in the introduction of a pair of forceps guided on the fingers, and the localization and extraction of the pin without previous dilatation of the sphincter ani, or the use of an anesthetic. Goodsall found it necessary to have recourse to a general anesthetic in quite a number of his cases, though it is to be noted that more than half of them were suffering either with an abscess or fistula when they came under his care.

The after-treatment consisted of frequent irrigation of the rectum with normal salt solution, which gave immediate and complete relief to all the symptoms. In case this had not given the wished-for results, mild antiseptic irrigations, consisting of thin starch-water, containing boracic acid, extract of hamamelis, or other mild antiseptic, would have been used, as we have found all of them quite efficacious in treating proctitis.

The appearance of a localized abscess in the rectal wall or in the perirectal tissues was closely watched for, but there were no signs of any trouble of this kind. Goodsall concludes "that when an abscess follows the puncture it begins to form within two or three days of the puncture." While this may be considered as a general rule, my case is an exception to it, as the patient had suffered with the acute symptoms for two weeks before coming to me. As a curiosity in this connection, I can also quote a case reported by W. Dutton Akers ("Pin in the Rectum for 30 Years," *Lancet*, 1898, Vol. II, p. 690), in which the patient had suffered for about thirty years with pricking pain in the rectal region on sitting down, constant desire to defecate, and pain on doing so. Besides this, the motions were small, pipe-like and streaked with blood. On examination, considerable induration and inflammation of the rectal mucous membrane were found. Above and to the right side of the internal sphincter, the head and half an inch of the body of a pin was felt, the head projecting upward and across the lumen. The pin was removed with dressing forceps, the removal being followed by rapid and complete cure.

An abscess or fistula is, however, probably the most frequent sequence, as Goodsall found in his twenty cases, three in which an acute abscess was present, while in ten there was either a blind or complete fistula.

If an abscess had been present it would have been freely opened, as is usual, and I wish to call attention here to the importance of thorough examination in all cases of abscesses, as several are reported in which the foreign body acted as an irritant, causing multiple recurrences.

In the case of a fistula, we have found it most satisfactory

to dissect them out carefully, after isolating the sphincter, close the bowel opening with catgut sutures after freshening its edges, and close the external wound with silkworm-gut. The precaution to search out and remove completely any branching fistulæ must be taken, as otherwise the wound will certainly break down.

A rapid healing will be noted after operation in these cases of fistulæ due to foreign bodies, with any form of operation, if the body is discovered and removed.

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SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

James J. Mills, M. D. Retinitis Albuminurica.—*Maryland Medical Journal*, August, 1900.

W. W. Ford, M. D., Ph. D. Chills in Typhoid Fever.—*Montreal Medical Journal*, July, 1900.

Hunter Robb, M. D. The Use of Rubber Gloves and Gauntlets as a Means of Preventing Infection in Surgery.—*Cleveland Medical Gazette*, August, 1900.

William Osler, M. D. An Address on the Importance of Post-Graduate Study.—*Lancet*, London, July 14, 1900; *British Medical Journal*, July 14, 1900.

Henry J. Berkley, M. D. The Pathological Findings in a Case of General Cutaneous and Sensory Anæsthesia without Psychical Implication.—*Brain*, Spring, 1900.

Eugene L. Opie, M. D. Pathological Changes Affecting the Islands of Langerhans of the Pancreas.—*Journal of the Boston Society of Medical Sciences*, June, 1900.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, June 18, 1900.

Report of Cases from Children's Clinic.

Case I.—*Tuberculosis following Syphilis.*—Dr. Amberg.

The short history of the case is as follows: A very emaciated colored child, male, 16 months old, with a strongly specific family history, came to the Dispensary with polymorphous syphilitic eruptions of the skin, beginning to appear several months ago, and also with fissures in the lips and ulcers in the mouth, suffering besides with malnutrition and rachitis. The syphilitic manifestations yielded readily to a specific treatment. The examination of the lungs, when first seen, only gave the symptoms of inflammation of the larger bronchi, later presented signs of consolidation of the right posterior part of the lungs. Dr. Booker made the probable diagnosis of tuberculosis guided by the fact that an uncle of the child, living with the family, had died a short while ago from consumption. The disease progressed rapidly and a few days later the child died, 18 months old. The temperature never exceeded 102°.

That syphilitic children acquire tuberculosis is not rare and in this particular case all the circumstances—syphilis of long standing, malnutrition, rachitis, and very bad hygienic conditions—prepared a very favorable soil for the infection.

The post-mortem revealed a disseminated miliary tuberculosis. Lungs, pleura, liver, spleen, kidneys and mesenterium are full of miliary tubercles. The pleura had on several places, particularly between the lobes, a thick fibrinous exudation. The trachea has in its lower part an ulcer whose sharply defined and not undermined borders do not show a very characteristic aspect, while lower down on the transition to the left bronchus is a more characteristic ulceration. The left bronchus opens immediately in a cavity nearly reaching the pleura. The bronchial glands are very much enlarged and the one cut open shows caseous degeneration. The rapidity of the course the tuberculosis assumed in this case, the formation of a cavity, the dissemination of the process and the great enlargement of the bronchial glands, make a picture which is not very seldom observed in children up to the second dentition.

Case II.—*Diphtheria with Cardiac Malformation.*—Dr. Amberg.

The second child, white, male, 15 months old, was brought to the Dispensary after having suffered for two days with a croupous cough. On the morning it was taken with severe attacks of dyspnœa, the pharynx was reddened, but without pseudomembranes or patches. A smear made from material taken from the pharynx contained diphtheria-bacilli. Blood-serum inoculated from the same material gave positive results. Dr. Booker performed an intubation, which gave relief after a short time, but the breathing was not perfectly free. Besides, the child got an injection of 1000 units antitoxin. The child remained under observation for 6 days, in which it got 3 times 1000 units of antitoxin. The fever was never high, the pulse always fairly good. The breathing was sometimes

free, mostly difficult, and the tube, which was several times taken out, had to be reinserted, but failed in the last days to give relief to any large extent. The examination of lung and heart was very difficult, owing to violent movements of the chest and the excitability of the child, but a bronchitis extending down to the finer tubes could be detected. The heart sounds were covered by the coarse bronchial râles.

The post-mortem gave the following result: The lungs were edematous, partly emphysematous with areas of bronchopneumonia. The division into lobes is abnormal, the right lung presenting an additional lobe. In the trachea we see the remnant of a false membrane immediately underneath the vocal cords—and two ulcers, one where the tube touched the anterior wall of the trachea and the other further up on the same side, in the height of the cricoid cartilage, not so extensive as the first but of the same aspect and very probably due to the tube too. The spleen has a small additional lobe.

But the most interesting features we find in the heart. The enlargement of the heart is best seen in comparison with the heart of the first child, who was 3 months older. The heart of this older child has a foramen ovale, which is not perfectly closed, but the opening is not very marked and can be demonstrated only by help of a probe. On the right side of the septum in the direction of the vena cava superior is a small pocket formed on one side by the septum, on the other by a thin membrane. It is about 1 cm. long and on the opening about ½ cm. broad. This opening looks downwards and its border consists of a muscular band. The other heart is enlarged as a whole, but the enlargement of the right side is preponderant. The walls of the heart are hypertrophic. Between the auricles is a wide opening crossed by several fibers coming from the posterior and superior walls of the auricles to the left of the middle-line and spreading fan-like to the anterior and inferior border of the foramen. The fibers are first muscular, but most of them become tendinous. The annulus interauricularis and the valvula foraminis ovalis, which form the secondary septum interatriorum are partly deficient, partly badly developed. The annulus interauricularis is running out in a muscular band, which you will see, holding the specimen towards the light, in the superior and posterior wall of the auricles. The origin of the above described fibers and what exists of the valvula foraminis ovalis is to the left of this muscular band. The valvula foraminis ovalis exists only in its upper part as a perforated membrane, showing the direction in which it should have grown by a few fibers. The opening is about the size of a silver quarter.

A remnant of the badly marked valvula Eustachii is to be seen in a fine ligament, running from the right side of the vena cava inferior to the also badly formed limbus Vieusseni. On the anterior wall, where the bulbus aortæ lies against the wall, are several muscular bands irregularly arranged, leaving small spaces between them, where muscular fibers are apparently wanting. There are no other irregularities to be noticed; the myocard and endocard seem to be in perfectly good order.

The occurrence of these large openings between the auricles without any other lesion of the heart is not frequent, as Peacock stated, and as it is particularly emphasized by Fallot, who found in the reports of 10 years of the Bulletin de la société anatomique and Bulletin des Hopitaux de Paris only 3 cases.

Two explanations are given for the malformations of the heart. One considers the malformation as a consequence of a fœtal endocarditis, the so-called anomalies subordonnées. I think we can rule out the fœtal endocarditis in this case, because there is nothing in the heart to justify this explanation, while the other irregularities found in lung and spleen lead us naturally to the other explanation and we may attribute the malformation to an arrest of development. Moussons is inclined to think, that perhaps too many cases have been ascribed to a fœtal endocarditis, recalling Rokitansky's experience, who found that alterations of myocard and endocard are rare or little marked in very young or still-born children, while more frequent and better marked in older children or adults afflicted with malformation of the heart. Further, Moussons points out that the endocarditis may be secondary, an idea already brought forward among others by Rauchfuss, who states that a malformation may give a predisposition for a fœtal endocarditis, explaining so that the fœtal endocarditis is oftener found in the right heart.

I will give shortly the way in which Rokitansky tried to explain the malformation in question, when there is, as in our case, no stenosis of the pulmonary artery. He argues thus: While the septum interatriorum is formed the septum interventriculare is not yet closed. If there exists now a malproportion between the pulmonary artery and the aorta, so that the aorta is relatively too narrow, a part of the blood of the left ventricle will flow through the opening of the septum interventriculare into the right ventricle, causing dilatation and relative insufficiency of the tricuspidal valve. There follows dilatation of the right auricle and of the part forming the transition from the right to the left auricle and the dilatation is made responsible for the prevention of the perfect formation of the septum interatriorum. After the closure of the septum interventriculare the left ventricle will become dilated and the walls hypertrophic. As the cause of the narrowing of the aorta, Rokitansky regards a failure of development. Rokitansky does not claim that this explanation is always found valid, saying, that there are cases where the septum interatriorum was found closed under more unfavorable conditions. In our case the circumference of the pulmonary artery in the valvular region—the heart was preserved in alcohol—is 4.5 cm., that of the aorta 3.0, while the corresponding figures of the other heart are 4.2 to 3.0 cm. If this condition allows the explanation, Rokitansky's is very questionable. He thinks it is important that the septum is generally pushed to the left, an impression we get undoubtedly in our case, so indicating, that it yields to a pressure exercised from the side of the right auricle.

Several etiological factors are claimed to be important. Heredity is made responsible in several cases direct or indirect; syphilis, tuberculosis, rheumatism, pneumonia of the parents were suspected in others. Besides we find accused marriages between near relatives, rachitis and nervous

diseases of the parents. Of all these etiological factors none can be made responsible in this case. Another fact remains to be mentioned, the child was never blue before it was taken sick with the attacks of dyspnœa. This confirms again the observation of the authors, who found that even a wide opening between the auricles is not necessarily followed by cyanosis. Fallot particularly has noted that the malformation in question only exceptionally leads to the "maladie bleue." It is well known that a malformation like this is not a danger to life and it may allow even hard labor. That the malformation of this heart is in any way connected with the fatal end, is doubtful. Nevertheless, it is probable that the already much enlarged heart had not the power of resistance, like a perfectly normal one, and that it succumbed therefore more readily to the diphtheritic virus and the weakening influences of the bronchopneumonia.

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Thrombosis of Carotid Artery.

DR. CUSHING.—The patient was a colored man, 52 years of age, who came in last fall with the diagnosis of a tuberculous ulcer in the bladder. He was operated upon Dec. 30, a suprapubic cystotomy being performed with the patient in the Trendelenberg position. The ulcer was excised and the wound in the bladder closed as is usual when there is no particular infection of the urine and nothing to indicate the necessity for keeping the bladder open. He made a very good recovery from the anesthetic and was left sleeping comfortably that evening. About midnight, however, Dr. Baer, who had him in charge, called me to see the patient, saying that he was stupid and dull. We found that he had a definite hemiplegia which we supposed was due to a cerebral hemorrhage. The left side of the face was completely paralyzed. The left arm was flexed and quite rigid, as was also the left leg. The respirations were Cheyne-Stokes in character. On the following day the whole left side became flaccid and he presented the characteristics of a hemiplegic. The paralysis of the left side was complete, except for the supraorbital muscle. For twelve days he went on without change in the symptoms; the bladder healed up completely and we supposed the paralysis would also clear up. On Jan. 13 there was a sudden rise of temperature with pain in the back of the head and neck. Lumbar puncture was made and clear fluid withdrawn; no cellular elements present and no organisms detected. Forty-eight hours after this exacerbation paralysis of the cervical sympathetic was apparent and on the next day a pronounced swelling of the whole upper extremity began and extended over the chest. We supposed there was a thrombosis of the jugular vein and that possibly it had extended downwards from the cavernous sinus. The patient gradually failed and died that night.

The pathological findings showed a thrombosis of the carotid artery and almost the whole right hemisphere was involved in a white softening. There was no apparent arteriosclerosis noted clinically nor at the autopsy.

Whether his position at the time of operation could have had any predisposing effect I do not know, but I believe that such post-operative calamities are practically unheard of on the gynecological side where that position is so frequently used.

DR. PATON.—On inspection of the external surface of the right hemisphere it can be easily seen even that there is a large area of softening. This area corresponds to the distribution of the Sylvian artery, leaving out the superior temporal and the superior frontal convolutions. On the inner surface the region supplied by the anterior cerebral is very firm and apparently not involved. The posterior cerebral supply is not affected. It is evident that the whole carotid area is not involved, but only that part of it which is supplied by the Sylvian artery.

The microscopic examination of the tissues brings out some interesting points. Sections taken from the right frontal convolution show no trace of nerve cells, but in their place are great numbers of cells similar to those found in all softened areas. One does not care to say anything definitely concerning the origin of these cells as it is an old question of dispute. Without doubt the vascular system supplied some, and the neuroglia tissue, others. Then there is a cell element that I believe will sooner or later be shown to have an important relation to these conditions, and that is the indifferent cell which exists in such great numbers in the adult nervous system. Some of these cells may persist as indifferent cells through life and some may become neuroglia cells.

The cells in the motor area on the right side show only very slight changes.

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ERRATUM.

In Dr. Welch's article, p. 186 (Vol. XI) of the BULLETIN, line 5 of foot-note 14, "constantly" should read "inconstantly."

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In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

REQUIREMENTS FOR ADMISSION.

As candidates for the degree of Doctor of Medicine the school receives:

1. Those who have satisfactorily completed the Chemical-Biological course which leads to the A. B. degree in this university.

2. Graduates of approved colleges or scientific schools who can furnish evidence: (a) That they have acquaintance with Latin and a good reading knowledge of French and German; (b) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study.

They are required to furnish certificates from officers of the college or scientific schools where they have studied, as to the courses pursued in physics, chemistry and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

Hearers and special workers, not candidates for a degree, will be received at the discretion of the Faculty.

ADMISSION TO ADVANCED STANDING.

Applicants for admission to advanced standing must furnish evidence (1) that the foregoing terms of admission as regards preliminary training have been fulfilled, (2) that courses equivalent in kind and amount to those given here, preceding that year of the course for admission to which application is made, have been satisfactorily completed, and (3) must pass examinations at the beginning of the session in October in all the subjects that have been already pursued by the class to which admission is sought. Certificates of standing elsewhere cannot be accepted in place of these examinations.

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Since the opening of the Johns Hopkins Hospital in 1889, courses of instruction have been offered to graduates in medicine. The attendance upon these courses has steadily increased with each succeeding year and indicates gratifying appreciation of the special advantages here afforded. With the completed organization of the Medical School, it was found necessary to give the courses intended especially for physicians at a later period of the academic year than that hitherto selected. It is, however, believed that the period now chosen for this purpose is more convenient for the majority of those desiring to take the courses than the former one. The special courses of instruction for graduates in medicine are now given annually during the months of May and June. During April there is a preliminary course in Normal Histology. These courses are in Pathology, Bacteriology, Clinical Microscopy, General Medicine, Surgery, Gynecology, Dermatology, Diseases of Children, Diseases of the Nervous System, Genito-Urinary Diseases, Laryngology and Rhinology, and Ophthalmology and Otology. The instruction is intended to meet the requirements of practitioners of medicine, and is almost wholly of a practical character. It includes laboratory courses, demonstrations, bedside teaching, and clinical instruction in the wards, dispensary, amphitheatre, and operating-rooms of the Hospital. These courses are open to those who have taken a medical degree and who give evidence satisfactory to the several instructors that they are prepared to profit by the opportunities here offered. The number of students who can be accommodated in some of the practical courses is necessarily limited. For these the places are assigned according to the date of application.

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